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PLENARY SESSION

The Pathology of the Tuberculosis

RELATOR :

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Problems of Tuberculosis Pathology

During the last years, much progress has been made in the field of prevention and therapy of tuberculosis (serial examination of the population with fluorography compulsory BCG vaccination, invention of efficient antibiotic and antituberculous drugs, development of lung surgery, etc). Our economical development has, with the assistance of the government aiming at the building-up of socialism, rendered possible that the progress of science and an enlightment work carried out on a large scale have resulted in the decrease of tuberculosis lethality by 73 per cent, as compared with 1938. The lethality of tuberculosis has, beside its decrease, exhibited a shift towards the older age groups. Whereas in 1938 only 19 per cent of the people who died of tuberculosis were over 50 years of age, their percentage was in 1953 46, nearly half of all cases. This immense development, and the pavlovian physiology gradually spreading into all branches of medicine, have brought about a qualitative change in our conceptions regarding the pathology of tuberculosis, and have significantly enriched our knowledge about that disease.

This review will deal with three main items ; viz.

1. The classification of tuberculosis,
2. the problem of reinfection,
3. some problems of tuberculous allergy and immunity.

1

The milestones in the classification of tuberculosis are the classifications of *Turban—Gerhardt, Bard—Piéry, Albrecht—Fraenkel, Aschoff—Nicol, Abrikossov,*

Haranghy, *Kováts*. The one adopted by the 5th Phthisiatric Congress of the Soviet Union, the proposition made by Rabukhin in 1953 as the plan of the Tuberculosis Institute of the Medical Academy of the Soviet Union, the plan of *Khmelnitsky* and *M. G. Ivanova*, *Strukhov's* motion at the congress held in Kuibishev, are discussed in detail.

In this country, pathologists have paid little attention to this problem, wherefore our classification of tuberculosis is far from adequate, as

a) it does not meet with the demands of clinicians. It is for this reason that at clinico-pathological meetings clinicians and pathologists employ two different languages ;

b) various classifications are employed by the pathologists themselves, depending on the institute (universities, departments of pathology at hospitals) where they work. As a rule, they adopt the classification of *Abrikossov* and that of *Aschoff* and *Nicol* ;

c) the classifications used in western countries and that of *Abrikossov* are of an anatomic character, taking into consideration merely the local tissue reactions. In this respect, classification is lagging behind the present clinical conceptions which regard tuberculosis as a pluriphasic process ;

d) the classifications hitherto advanced consider mainly the grave forms, whilst the early processes which are of a decisive importance, especially in preventive work, have not been listed by them ;

e) the classifications used, probably under the influence of virchowian pathology, do not emphasize the fact that tuberculosis is always a disease of the whole organism ; they do not reflect the dynamics of evolution, nor the reversible or irreversible character of the changes.

An uniform classification is therefore needed. To this end, the Association should form a committee for the preparation of an uniform anatomo-pathological classification of tuberculosis. This committee should take into consideration the classification accepted by the 5th Phtisiatric Congress of the Soviet Union and *Strukhov*' s plan. After the pathologists have attained an agreement, they should discuss the problems with clinicians.

Every classification is incorrect if it gives a mere scheme without reflecting the pathogenesis of the disease. It would, therefore, be incorrect to discuss classifications without being concerned with the problems of pathogenesis. This is why in this review we shall discuss the recent conceptions about the pathogenesis of tuberculosis, with special stress laid upon the work of *Z. Lebedeva* et al. According to this concept, the primary focus is not identical with the first localization of the pathogenic agent, from where the process may spread. The primary complex (focus) is merely the clinically and morphologically best observable manifestation of a general dissemination taking place in all cases.

2

The terms »reinfection« and »superinfection« must be defined correctly, there being much uncertainty in their use.

Superinfection is called a new infection associating itself with an already existing tuberculous infection. This often gives rise to the exacerbation of the process. On the other hand, reinfection means a new infection occurring at a time when the disease caused by the previous infection had already healed. True reinfection is rare. It occurs mainly in advanced age. It imitates the morphological picture of the primary complex. It is for this reason that in old age some cases of tuberculosis display much clinical, pathogenetical, and morphological similarity to children's tuberculosis. Tuberculosis due to reinfection is accordingly not identical with secondary tuberculosis, though these terms are often misused for one another. The misinterpretation originates from *Aschoff* and his followers who, while examining the mechanism of the evolution of adults' focal tuberculosis, called attention to the chronic foci in the lungs and claimed that these »reinfection foci« have nothing in common with primary ones and are sequels of exogenous reinfection. *Abrikossov* ascribed similarly to exogenous reinfection the earliest postprimary focal changes, such as endo-, peri- and panbronchitis. On the other hand, Soviet researchers have, by means of complex examinations, revealed relationships between children's primary tuberculosis and adults' focal tuberculosis and at present a great number of authors agree with *Strukhov* in that focal tuberculosis in the adult develops most frequently by an endogenous route. Whether of endogenous origin or exogenous origin, the initial tissue changes in focal tuberculosis are identical with those described by *Abrikossov* and the process goes on in both cases on the new immunobiologic ground brought about by the primary infection. It is just for the latter fact, that, while emphasizing their close correlation, primary and postprimary processes should sharply be separated. This is why the old classification into three stages has been replaced by the modern one distinguishing only two stages of development.

3

The problems of tuberculosis allergy and immunity have led to much confusion. This is partly due to the fact that, under the influence of virchowian cellular pathology and Ehrlich's humoral pathology — these concepts based on mechanical materialism and philosophical idealism, — immunology and allergy have become independent of physiology. Immunologic research has been restricted to test-tube experiments, allergy to the examination of skin phenomena. These tendencies resulted in that phenomena of tuberculous allergy and immunity were regarded not as symptoms of the organism's reactivity, nor were they

examined by means of physiologic methods beside the immunologic ones but were considered as phenomena *in se*. In addition, natural resistance and acquired immunity were regarded as terms opposite to one another and there was no answer to the question of the relation of allergy and immunity.

On the basis of progressive Soviet biology and pavlovian physiology, these problems have been essentially clarified. Tuberculosis is not simply the result of a fortuitous meeting between the organism and the pathologic agent. The agent represents an „extra-stimulus". Like other stimuli, the organism adapts itself to it first of all by reflex functions. At the same time, the central nervous system may also become damaged by the infection. Adaptation will be secured by mobilizing the defensive mechanisms. The mechanisms of natural resistance are in general characteristic of the animal species. The resistance of the individual subject depends, however, on various circumstances, in man especially on social conditions. Acquired immunity is, in return, characteristic of the subject, rather than the race, and its defensive mechanisms are not independent, but act by enhancing the function of the same mechanism on which natural resistance is also based. Acquired specific immunity is thus closely related to natural resistance. Allergic (hyperergic) phenomena too are due to defensive mechanisms which, however, owing to the lesion of the central nervous system, become exaggerated in this case.

Accordingly, the phenomena of natural resistance, immunity, and allergy, are all due to defensive (immune) mechanisms controlled by the central nervous system: they are closely related different categories of the reactivity of the organism.

On the present level of science, defensive mechanisms cannot be studied but on a pavlovian basis.

CO-RELATOR:

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Pathological Anatomy of Pulmonary Tuberculosis, on the Basis of Resected Specimens

The removal of lung parts has supplied pathologists with much valuable material during the last decades. It has made it possible to examine pulmonary processes during the progression and regression of tuberculosis, and also to study the effect of therapeutic measures. In the following, only the tuberculosis of adult age should be dealt with: neither the changes occurring in children, nor generalized' adults' tuberculosis, will be discussed.

In the surgical department of the Korányi Tuberculosis Sanitarium, resection of a lung or a lung part was, from 1952 to date, performed in 310 cases. Both severe and initial changes occurred mainly in the anterior and posterior apical and the 1st dorsal segments. The latter localization is often due to progression or bronchogenous dissemination from the two former ones.

The localization is independent of the source of infection. In *Pagel's* experiments, sensitized rabbits developed tuberculosis in the cranial lung areas after both intravenous and intrabronchial infection. True exogenous infections result also in processes of the anterior and posterior apical segments *(Terplan)*. This localization has induced Kalbfleisch to claim that tuberculosis spreads in the dorsoventral, rather than the apico-caudal, direction. On the other hand, bronchogenous phthisis starting from a primary focus may set on in the basal segments, and so may initial processes associated with deformity of the thorax or aspecific carnification.

The division into exudative and proliferative forms of tuberculosis being inadequate to convey the variety of processes, in the following the grouping employed by Soviet pathologists will be used.

I. Phase of infiltration. The first microscopic change is aspecific pneumonia. Caseation and tubercles arise at a later time. Wurm distinguished 3 phases of the infiltrating process. (i) Increase of exudative cell elements and tubercle formation, (ii) aspecific inflammation containing mycobacteria, (iii) perifocal inflammation.

Caseation is a transition from the infiltrative phase to the phase of destruction and dissemination, and, in the normergic organism, it is a primary process. In the sensitized organism, infiltrative-exudative or proliferative granulation areas undergo caseation. The type of caseation cannot be definitely determined from the behaviour of the elastic fibres. Beside allergic processes and the bacteria other factors too play a role in caseation. As against earlier description, intact vessels are frequently found in caseated areas.

II. The phase of destruction and dissemination is characterized by acute inflammatory changes. In Wurm's wording, destruction is a caseous necrosis imbibed with inflammatory oedema.

III. Restoration takes place by absorption and condensation. They are, like initial exudation and proliferation, inseparable simultaneous phenomena. Antibiotic treatment. while it resulted in the abbreviation of the restoration processes, did not change their morphology, so that the number of aspecific complications has increased. Fibrosis and condensation do not mean in all cases healing, they may occasionally give rise to destruction and to impairment of the respiration and the pulmonary circulation. Fibrosis may arise, beside the tuberculous areas also in those of congestion and aspecific inflammations.

As to the changes characterizing the single phases, they are rarely isolated but mostly only prevail in the process. Therefore, various phases may be

pathogenetically related to each other. On the other hand, there is little, or no correlation between morphology and the time at which the process had set on.

According to the Soviet nomenclature, adults' tuberculosis starts with one of the following forms : subacute-chronic haematogenous dissemination, nodose tuberculosis, caseous pneumonia, circumscribed infiltration. This grouping is based on gross appearance only and admits, aside from the case of haematogenous dissemination, no conclusion as to the pathogenesis.

Cavity formation is a relevant factor in tuberculosis. The grouping of cavities according to *Schmincke* has been discarded. The wall of the cavity undergoes marked changes in the course of treatment. During extensive absorption, thick walls may become thin. Their thinning may also be due to caseation involving the outer layers. The following types may be distinguished, partly according to shape and wall thickness : (i) Cavity with a thin wall, mostly due to colliquation. (ii) Cavity with a thick wall developed through sequestration or through fibrosis of a thin wall. (iii) Lobular cavity, i. e. a system of irregular cavities (»wormeaten«) deriving from confluent caseous pneumonia. (iv) Tuberculous bronchiectasic cavities. (v) Vomicas, due to colliquation of acino-nodose foci.

Filling of a cavity may occur if the draining bronchus is closed and the exudate becomes absorbed. Restitution is, as a rule, simultaneous with the closure of the bronchus. The latter is, however, often temporary if the exudative processes persist.

The filled cavity is one of the forms of tuberculoma. Other forms are an encapsulated primary focus, or postprimary caseous pneumonia, or confluent tuberculous nodes. The tuberculoma is mostly solitary, in 10 per cent of the cases multiple *(Rüttiman)*. As a rule, it is the predominating change, in other cases a partial phenomenon of bronchogenous phthisis.

Following cavity formation, progression takes place by continuous spread or remote bronchogenic dissemination. Pericavernous foci may, however, be produced by nodose tuberculosis. Pericavernous extension of the process may sometimes lead to massive tuberculous pneumonia.

Remote bronchogenous disseminations from a cavity or a liquefied nodose process are often found at the lower margin of the upper, or the upper margin of the lower lobe, in the 1st dorsal segment, and the lingula. Its elementary phenomenon is acino-nodose tuberculosis *(Aschoff—Nicol)*.

Recently, attention has been called to the tuberculous diseases of the bronchi. According to the Soviet nomenclature, bronchial tuberculosis is a complication. Changes in small bronchi form an additional process to those of the parenchyma. Involvement of the segmental and subsegmental bronchi renders the process more serious. The following forms occur : (i) Caseous bronchitis. The lumen is filled with a caseous mass, the deeper layers show little change. It is usually associated with grave bronchogenous disseminations

and cavity formation. (ii) Proliferating bronchial tuberculosis. The layers of the bronchial wall are involved to a varying degree. The most frequent forms are submucous tubercles and tuberculous peribronchitis. (iii) The most severe form is a tuberculous ulceration, due, as a rule, to perforation of a diseased lymph node into the lumen, or else it may also develop from forms i) and ii). *Schwarz* holds that caseous lymph nodes perforating into bronchi play a predominant role in the pathogenesis of pulmonary tuberculosis.

The morphology of tuberculosis is further influenced by aspecific complications, such as fibrosis, bronchiectasis, emphysema, atelectasis, collapse induration, and carnification. The final result may be complete destruction.

As a rule, the tuberculous process does not pass through all of the above phases. Its spread always takes place by acute inflammations, exacerbations. As seen from the removed specimens, the process may for a very long time be limited to one side or to a circumscribed area. The following differences are shown by material from operation in comparison with specimens removed at necropsy.

(i) They represent intervening forms, (ii) frequent aspecific complications due to therapy, (iii) rare occurrence of acute changes, (iv) they yield a basis for appreciating previous therapeutic measures.

CO-RELATOR:

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Nervous Relationships in the Pathology of Pulmonary Tuberculosis

Numerous previous observations especially those concerned with the detection of virulent bacilli in normal organs, and the restitution of tuberculous pneumonia despite the presence of living bacilli, support the view that the decisive factors in the evolution of tuberculous disease should be sought in the macro-organism rather than the microorganism. More recently it has been shown that immediately after the infection tubercle bacilli give rise to reflectoric disorders of vasoregulation, qualitative changes in the blood-count, especially leucocytosis *(Ricker* and *Goerdeler, Kán* et al.). These findings support, at the same time, the observation that leucocyte reactions may be due to reflexes *(Borchardt, Rosenow, Wespi)*. Physiologic leucocytosis is ensured by cortical-subcortical co-operation *(Lissák et al.)*. The neurohumoral regulation of phagocytosis by leucocytes and the role of neuroreception in this process have

also been recognized *(Kutchak, Yaroshevsky, Benetato, Ludány* et al.). Many authors have emphasized that the phagocytosis factor in tuberculosis must not be disregarded in the analysis of complex defensive mechanisms *(Rist, Leon, Kindberg, Rolland, Takeuchi)*.

The neurohumoral regulation of the reticuloendothelial system, as elucidated by Soviet authors and by Törő, Karády et al. plays an important role in tuberculosis. *Kutchak* and *Dravkina* have demonstrated that phagocytosis of mycobacteria by the reticuloendothelial system is under central influence. As to this, views are still divergent, probably because of difficulties of methodology and further examinations are necessary to clear the problem.

The barrier function of tissues *(Bermann, Krause)* has not yet been investigated in respect of its neural regulation, though the effect of the pituitary-adrenal system *(Gell and Hind, Tonutti,* etc.) on this function and of the premamillary region of the hypo-thalamus *(Mess* and *Endrőczy, Irányi* and *Kovách)* upon this latter humoral apparatus are well-known.

Moro, Dolfini, Mikhaylovsky and numeorus other authors succeeded in modifying the tuberculin test, this approximative indicator of tuberculous allergy, by means of influencing the central or peripheral nervous system by chemical substances or operative methods. *Levendel* et al. found a parallelism between the *Mantoux* test and the functional state or phase conditions of the cortex in protracted sleep, mental disorders, and hypertension. It having been ascertained that in the allergic organism tuberculin brings about alterations in certain vasomotor reactions, it may be assumed that the intense vasomotor reaction in hyperergy (perifocal inflammation) are manifestations of the increased excitability of regulation. It is on these facts that *Ickert*'s thesis has been based, viz. that a diencephalic dysfunction is responsible for the exacerbations and different hyperergic reactions in tuberculosis.

The trophic function of the tissues may be profoundly disturbed by innervation disorders *(Asher, Orbeli, Speransky, Cannon, Ken Kuré)*. In the complex process of the tissues' adaptation to bacteria neurohumoral factors regulating homeostasis play a prominent part. During protracted tuberculosis the nervous system sustains damage. The damage, of which there is often morphologic proof *(Yarughin, Moghilnitsky, Puzik)*, gives rise to so-called vegetative dysfunctions and also influence the evolution, localization, and form, of the specific process. This may explain the success of early neurotomy for laryngeal tuberculosis *(Spies* etc.), the control of tuberculous dissemination by vagotomy, or the stimulation of pulmonary receptors *(Speransky et* al.). The mechanism of the early control of tuberculosis following microlesions of the tuber cinereum may also be evaluated in this sense *(Kurucz, Polgár)*.

The problem of the localization of pulmonary tuberculosis has not yet been cleared. Apart from the theory of local immunity (Davidov), and those based on haemodynamical and aerodynamical factors or on autoallergy, *Kalbfleisch's*

theory deserves special attention. In the opinion of this author pulmonary innervation is an important factor in the localization of the process. *Kalbfleisch* adopted *Reinhardt*'s thesis on the metameric innervation, according to which lungs are divided, apart from the so-called bronchopulmonary anatomic segments, into metameric, neural functional segments, similar to the dermatomes. The latter segments are girdle-like and horizontal, and overlap the borders of the lobes. Where their functional innervation is not uniform, pathologic processes may display a neurosegmental horizontal localization, as is not infrequently the case with vasoregulatory disturbances of cerebral origin, haemorrhage, atelectasis, and even with "lobar" pneumonia which former is often bilateral and symmetrical. Similar processes may be induced experimentally as well. Anatomical research has not yet produced any onto- or philogenetic evidence supporting this kind of innervation, nor has the course in the lungs of spinal nerves been traced. Neither can the theory explain the fact that the levels of horizontal pulmonary changes brought about by severing the spinal roots do not correspond to the innervation levels of the same roots. The concept of the metameric spinal innervation of the lungs has, therefore, no other basis for the time being than some experimental findings *(Rein hardt, Kalbfleisch* and *Herzklotz, Leschke)* and pathological observations *(Fleischner, Sturm)*. These, comfirmed by our own experiments, however, support the assumption that, as regards spinal innervation, there are in the lungs horizontal areas lying in the same level which constitute a neuromuscular and neurovascular functional unit independent of the lobe borders.

Kalbfleisch gives the following summary of the spread and localization of phthisis ; (i) Chronic phthisis spreads often through horizontal segments in apico-caudal direction. The changes are frequently symmetrical on both sides and belong to the same type within one segment, but differ sharply in different segments. (ii) The spread is often discontinuous. (iii) Continuous spreading may take place within the same segment in the dorsoventral direction, so that anteriorly situated changes are more recent. If it is warranted to draw conclusions from the localization of phthisis and the localization of pulmonary changes developing after neurotomy, it seems that the pathologic process is greatly influenced by the functional state of pulmonary innervation, as clear particularly from the fact that large pulmonary areas may be spread over with bacilli and still remain healthy, with the disease at the same time appearing in symmetrical horizontal segments. This is further supported by the observation of *Kalbfleisch* on the horizontal localization of silicosis.

The pathogeny of atelectasis too is being ascribed to mechanical and nervous factors. On the basis of up-to-date conceptions, contraction atelectasis of reflex origin *(Sturm)* may be considered a defensive reaction which, however, may give rise, in case of increased irritability, to inflammatory changes

owing to the disturbed circulation and ventilation of atelectatic areas, unfavourably influencing in this way the disease.

Summing up, the evolution of tuberculosis is, through several factors, greatly influenced by the organ securing the dialectic unity of the organism and its environment, the central nervous system. This final conclusion is based on the immunologic and allergic reactions observed in tuberculosis, and on the intrapulmonary localization of the disease.

DISCUSSION

Localization of Lung Segments in the Regional Lymph Nodes

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Human and animal pulmonary segments were compared on the basis of *Kassai* and *Guzsai*'s classification. The topography of the lymph nodes was examined in 25 dogs. The result show that conditions in man differ only numerically from those in the dog, while there is no difference in localization. The examinations were carried out by insufflating into certain segments powdered soot by means of a bronchoscope, and 2 or 3 days later the lymph nodes were examined in preparations cleared up by *Spalteholtz*' s method for the presence of soot. In order to examine segments inaccessible to the above method (upper lobes, left lingular segment, the dorsal 1st and 2nd segments on both sides), the chest was opened and Indian ink was injected into the pulmonary parenchyma.

It became possible in this way to determine the localization in the corresponding lymph nodes of the single segments. The localization of two segments of intermediary lobes supports *Kassai*'s view that they correspond to the basal medial segment of both lungs, since their lymph vessels pass from them to both the right and left laterotracheal lymph nodes.

There is a segment-like differentiation also within the individual lymph nodes, probably as a remnant of the fusion of primary nodules. It is therefore hoped that by further studies it will be possible to determine the localization of segments within the regional lypmh node.

As to the problem whether the lobe or the segment should be considered a unit in lymph drainage, it is thought that under physiological conditions each segment constitutes an independent unit. Under morbid conditions (congestion) they become fused so that the lobe will become the unit.

Periarterial Lymph Spaces in the Lung

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In 1940 *Hayek* reported on lymph spaces surrounding the arteries of the human lung. The spaces were rendered visible by fixation from the trachea. Though such lymph spaces had repeatedly been described in animals, *Maraschio* considered the structures found by Hayek artefacts. Since then the existence of the spaces has gradually been adopted. The preparations now demonstrated derive from different pathological cases. The spaces are well visible. No similar spaces have been found around the veins. The periarterial lymph spaces have the function to render arterial circulation independent of the changes of intrapulmonary pressure.

Evolution of Bronchopneumonia Following Bilateral Vagotomy

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To date, only the fully developed pneumonia due to bilateral vagotomy had been examined, never the evolution of the process. — In 17 rabbits bilateral cervical vagotomy was performed. The animals were killed, through air embolism, ½, 1, 1½, 2, 3, 5, 8, 18 hours, respectively, after the operation. Following results have been obtained. After 30 minutes a few red corpuscles and leucocytes appear in the interstitium. After 1 hour both elements occur in the alveoli. After 90 minutes focal haemorrhages and leucocyte infiltrations involving from 10 to 15 alveoli are seen and focal oedema appears. Then the foci expand and, after 8 hours, pneumonia foci extending over two thirds of the lung surface are visible to the naked eye. — Aspiration was observed in 7 cases, mostly without an inflammatory reaction. — Since the onset of inflammation occurs as early as after 30 minutes, while focal oedema does not appear before 90 minutes, it is thought that the pneumonia is due to dystrophic processes caused by innervation disorders, rather than to a pressor effect.

Topography of Lung Changes Following Neurotomy

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The experiment was performed on 32 healthy and 73 tuberculous guinea pigs. The tuberculosis of the animals was very mild, their majority displayed no pulmonary change. In ether anaesthesia unilateral cervical vagotomy was carried out in 22 animals, a lesion of the dorsal vagal nucleus in 10 animals. In the control group either the hypothalamus was injured or the environment of the vagal nuclei, or only anaesthesia was employed. The following changes have been revealed in the lungs removed in ether anaesthesia after 24 hours. Pulmonary changes were present in 12 out of 22 vagotomized animals and in 9 out of the 10 guinea pigs in which the vagal nucleus had been injured. Out of 75 controls only 3 displayed similar changes. The changes consisted in punctiform haemorrhages contraction atelectasis and early pneumonia. This occurred mainly, or exclusively, in the apical and infraclavicular areas, sometimes on both sides. With the special infection technique of Pagel tuberculosis similar to the human disease was brought about. This showed the same localization as the above condition. It seems therefore, that disorders of the vagus system probably have a role in the onset of early infiltrations.

Stereo-Examination of the Normal and Morbid Structure of the Lung

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The methods devised hitherto for the examination of the lungs are in many respects unsatisfactory, since they give no means for stereo-examination of the single parts of the lung. The procedure described below completes earlier methods and renders stereo-examinations possible.

All blood causing the organs to become rigid and brittle should be removed from the vessels by irrigating them with physiological salt solution. Then the organs are injected through the vessels with a 4 per cent formaldehyde solution and fixed in the same fluid. After fixation the organs are washed and imbibed with glycerin. 40 to 50 ml of glycerin is needed for one lung. Then the organs are placed into a vacuum vessel in a way that their air passages and their vascular system should be in free air.

Within a week the lungs will display the following properties. They may be preserved without a preserving fluid. They are and remain soft and elastic and they do not shrink. Unlike the preparations preserved by treatment with carbolic acid—glycerin, they are dry to touch. Unlike the preparations saturated with paraffin they are neither rigid nor brittle whereby they may be injected or examined by any method, like a fresh organ. The organ will not become distorted, its shape remains identical with its original one, including the full preservation of its superficial impressions, grooves, lobular design, etc.

The structure of these lungs can be examined with a stereo-microscope, i. e. in space. In this way it becomes possible to form a more correct concept about the structure of the organ, than the one based upon examination of a few sections. Special importance should be attributed to this fact in teaching anatomy. The alveoli, alveolar ducts, respiratory bronchioles, acini, lobules, arteries and veins, may be visualized in space, and their interrelations during the various phases of development, under normal and pathologic conditions, can be studied.

The different parts of the lungs can be cut into sections of varying thickness and in this way a reconstruction model may be prepared. The procedure is particularly advantageous for the study of the physiological and pathological conditions of the lung segments.

Congenital Tuberculosis, on the Basis of a Case

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Report of a case of congenital tuberculosis diagnosed during life and examined post mortem. At the time of the delivery, the mother had suffered from subacute miliary tuberculosis. Her male infant died at the age of two and a half months. At necropsy a partially calcified primary focus was found in the liver and in a lymph node of the hepatic hilum. Beside this, submiliary foci were present in the liver, spleen, lungs, lymph nodes, and suprarenal glands. The Mycobacterium has been demonstrated by animal inoculation. Genesis and pathology of congenital tuberculosis are discussed in connection with the case reported.

Pulmonary Tuberculosis and Lung Cancer

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126 cases of lung cancer deriving from operation and necropsy material have been examined. In one of them a cavity cancer was present. In such cases a squamous cell carcinoma is usually found although *Kostka* observed a small cell cancer starting from a tuberculous cavity. In *Attinger's* view cancer accompanying tuberculosis may start from the bronchus draining the cavity.

One of the present cases suggested that the neoplasm may interfere with the resistance of the organisms and gives rise to the activation of tuberculosis. On the other hand, cancer may also develop on the basis of long-standing tuberculosis.

Scar cancers *(Friedrich* and *Rössle)* arise in peripheral parts of the lung, in scars near the pleura. Their significance has been emphasized by *Lüders and Themel.* Their site is frequently a cicatrized primary infection or reinf. ction.

The three cases of scar cancer observed by the lecturer were of the alveolar-cellular type.

60 tuberculous lungs were histologically examined. The flat alveolar epithelium may become cuboid or cylindric and begin to proliferate in the neighbourhood of a specific focus. Another change occurring with tuberculosis is squamous cell metaplasia.

The neoplastic effect of some drugs can be experimentally demonstrated. Out of the antituberculous drugs, INH has been supposed to exert a cancerogenic effect.

The Problem of Tuberculosis in Old Age

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The tuberculosis of 34 subjects beyond 50 years of age was thoroughly studied. 10 subjects were in the 6th decade, the others were beyond 60 years of age. The age of the two oldest ones was 81 and 82 years, respectively. Tuberculosis had been recognized during life in as few as 10 subjects. 10 of the 24 subjects belonging to the undiagnosed group had simultaneously a malignant tumour. The following results have been obtained.

Tuberculosis is more frequent in old age than is believed by general practitioners. The majority of cases is sent for a postmortem for other diseases than tuberculosis, since tuberculosis in these subjects had ensued after, or in the society of another disease. Stress should be laid upon the fact that malignant growths are frequently associated with tuberculosis. In most cases it seems that the deteriorated organism was attacked by mycobacteria which had been present in it in a stage of latent microbiosis. The source of infection may be an apical focus containing though encapsulated and surrounded by a calcified coat, living mycobacteria, or a calcified lymph node. In 2 cases exogenous superinfection was assumed. The form of the process was in these subjects similar to the generalized tuberculosis of children. — The infection was in all cases partly due to the weakening of immunobiologic reactivity.

Development of Tuberculosis in Children

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In a 4 month old infant the transplacentar origin of miliary tuberculosis could be demonstrated by finding the route of the infection in the lig. teres, porta hepatis, and lungs. The earliest postnatal tuberculous foci may be found anywhere in the lung characterized by tissue anergy: most frequently small paravertebral atelectasic foci, circumscript hypoplastic foci, and, occasionally, infantile adenomas, like in the case demonstrated. Histobiochemical examinations have been carried out, first in infants, then in older children, with the result that the fibrous-caseous transformation of the specific granulation tissue is partly due to the fixation of hyaluronic acid, whilst progression, liquefaction, and exudative exacerbations are mainly produced by hyaluronidase action. These facts may be useful in the therapy of infantile tuberculosis. In the high tuberculosis morbidity and mortality of premature and dystrophic infants, hypoxsemia and an excess of gonadotropic hormone demonstrated by biomorphological methods may have a role. Animal experiments were performed in order to prove the above statement.

The Pathology of Tuberculoma

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»Round shadows« in the lungs are observed with increasing frequency. Earlier these shadows had been designated with the collective term tuberculoma, irrespective of their pathological basis. After surgeons began to remove them, it has been learned that their structure is not uniform. Fusion of small caseous foci a larger caseous focus, overlapping caseous and fibrous layers equally give the picture of tuberculoma on the X-ray screen. Modern chemotherapy, especially treatment with INH may lead to the formation of filled cavities which, too, appear as round shadows. In this manner pathologically entirely different structures have clinically been designated with the term tuberculoma.

The authors examined all tuberculomas removed within the past years. Results of their gross and microscopic examinations are reported and illustrated by slides. On the basis of the examinations it was concluded that structures presenting the roentgenologic picture of tuberculoma may originate through various mechanisms and may, accordingly, exhibit pathological differences. Independent of their origine some signs of activity can be recognized in the histological structure: the standing control of nonoperated cases is necessary too.

Correlation of Vitality and Pathogenicity of Mycobacteria

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It is well-known that local application of killed mycobacteria may lead to tissue changes characteristic for tuberculosis. There are, further, mycobacterial extracts which act as a chemical factor and produce on local application characteristic tissue changes. The spread of tuberculosis, i. e. the tuberculous disease is, according to general opinion, the effect of living bacteria. *Thomson* in 1932 was the first to produce generalized tuberculosis with killed or apathogenic mycobacteria.

The authors have repeated these experiments with the same result. In order to produce generalized tuberculosis, at least 20 to 30 mg of dried and killed mycobacteria mixed in 1 ml of paraffin oil had to be injected in rabbits testis.

It has been demonstrated that entry of living virulent mycobacteria is not indispensable for producing generalized tuberculosis; under certain environmental or other conditions, killed or apathogenic bacteria are also capable of bringing about generalized disease. Thus, the main factor of the disease is a nonliving chemical substance, rather than the living bacterium. These results are extremely important, and apart from their pathological significance they should be taken into consideration at examinations concerned with the mode of action of antibiotics. Presently, bacteriostasis, i. e. the effect on the living germ, is regarded the decisive factor in antibiotic therapy, whilst the organotropic and detoxicating actions of the antibiotics are usually considered a secondary factor. The authors hope that the described experiment, as a biological test, is suitable for settling this problem. The results of further studies will be reported shortly.

Comparison of General and Organ Tuberculin Oversensitivity in Tuberculoallergic Rabbits

Gy. Szabó

(City Hospital, Makó)

0,1 ml of a tenfold dilution of a culture of human mycobacteria was injected to 7 rabbits each into the anterior chamber, to 7 other subdermally, and to 2 animals into the anterior chamber *and* subdermally. 4 rabbits received no treatment.

In the 7th week following the inoculation, i. e. at a time when tuberculo-allergy had already developed, as shown by the presence of a tuberculin ulcer and focal reaction, serial tuberculin inoculations were made under the conjunctiva of the diseased eye, further subconjunctivally in the healthy eye of all rabbits, finally intradermally, on the inner smooth surface of the ear, to all rabbits. The animals were killed and examined in the 7th month. In all infected eyes and in the lung of 2 rabbits characteristic sign of tuberculous inflammation were revealed.

Results. 1. If only the anterior chamber had been infected, the oversensitivity to tuberculin of the eye was markedly higher than that of the skin. — 2. There was a slight difference between the oversensitivity of the diseased and the healthy eye. The sensitivity of the healthy eye increased to a greater degree than that of the skin. — 3. In the animals which had been injected at the same time subdermally and intraocularly, the allergic conditions were the same as in those which had been inoculated into the anterior chamber only. — 4. In the rabbits treated with subdermal inoculation only, there was no marked difference between this sensitivity of the eye and the skin, both being significantly lower than the sensitivity of the diseased eye.

The results support our clinical observations and assumptions that

1. In circumscript organ tuberculosis the tuberculin sensitivity of the diseased organ is, as a rule, higher than that of the skin. — 2. If one of a pair of organs is afflicted with a tuberculous process, tuberculin sensitivity is in most cases increased also in the twin organ. — 3. It is of a practical importance that a mild response to an intradermal test may, owing to the increased organ sensitivity, give rise to harmful focal reactions in the organ in question. — 4. The difference existing between the sensitivity of the skin and the organs could well be used for diagnostic purposes. The sensitivity of an organ higher than that of the skin points to tuberculosis in that organ.

Experimental Influencing of Tuberculous Changes

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In guinea pigs infected with virulent human strain of mycobacteria it was tried to influence the development of tuberculous allergy by means of various kinds of aspecific treatment. The state of allergy was judged from the reaction to tuberculin and the gross and microscopic changes of the organs. By acting upon the neurohormonal apparatus the development of a positive skin reaction to tuberculin could be prevented or weakened. At the same time, the specific changes in the organs were more marked than in the control animals.

Vascular Changes in Experimental Tuberculosis of Guinea Pigs

I. Földes

(State Tuberculosis Institute, Budapest)

Guinea pigs were inoculated with small doses (0,001 mg) of human Mycobacterium tuberculosis. 3 to 4 month later the animals which did not die spontaneously were killed. Besides the well-known vascular changes the following were found. (i) The wall of the large arteries becomes loose, its elastic fibres disintegrate, become thin, fragmentation and complete destruction occur whereby unstained spots appear. This fact is in agreement with the earlier observation of *Kálló*, that the changes in the aortic wall found at necropsy of tuberculous patients are due to the disease rather than old age. It seems that the elastic system is damaged by tuberculosis. The same effect may play a role in cavity formation. (ii) The wall of the small and middle sized hepatic veins is thickened, partly hyaline. The lumen is partly or totally filled with granulation tissue of circular arrangement. These changes in the hepatic veins may occur near to, but also far from, tuberculous foci. The changes observed differ from *Weigert's* endophlebitis tuberculosa and also from the intima granulomas described by *Siegmund*.

Effect of Nitrogen Mustard on the Histologic Structure of Tuberculous Lymph Nodes

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(State Tuberculosis Sanitarium, Debrecen)

Considering the literary published favourable effect NM exerts on tuberculous lymphadenitis, the purpose was set to evaluate the effect of this treatment and to determine the mode of action of the drug. To this end, lymph nodes excised from patients at the end of the cure were examined. In part of the patients some clinical improvement was indisputable. Histology revealed vacuole formation, or, to some degree, filametous transformation in the cytoplasma of *Langhans'* giant cells. Where a high total dosis of NM was administered only a few, or no giant cells have been found in the otherwise typical tuberculous granulation tissue. — The biological explanation of this observation is at present not satifactory.

Non-specific Tissue Reactions in the Lymph Nodes of Tuberculous Guinea Pigs

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(Tuberculosis Department, Medical University, Budapest)

In the experiments, 110 guinea pigs weighing from 300 to 600 g were used. Each experimental animal was given in the preliminary experiment 0,1 mg, and in the proper experiment 0,25 mg, of a 14 days old culture of the strain H 37 Rv subdermally, into the inguinal fold. They were treated with adequate therapeutical doses of INH and streptomycin. One group of the

animals was treated simultaneously with the infection, the other after the tuberculous process had developed. Infected untreated animals, and healthy ones treated with INH and streptomycin served as controls. Out of each group an identical number of animals were killed with ether at various stages of the infection, in the 3rd, 6th and 12th weeks.

Gross examination and histology have shown that the severeness of the tuberculous changes within the individual groups was more or less identical.

The results obtained were as follows.

(i) As a rule typical aspecific tissue reactions were found in the lymph nodes and the spleen. Their extent depended on the progression and spreading of the infection. The early stage of generalization (3rd week) was characterized by a reticulum cell reaction in the regional lymph nodes around the portal of entry. In more remote lymph nodes the increase of plasmablasts was the more common. With time, the plasmacellular reaction increased and exhibited a shift toward more mature forms (6th to 12th week). As for the lymphoid elements, diffuse lymphoid hyperplasia set on initially, whereas the later stages were characterized by a mild damage to, and inactivity of, the lymph follicles and elements.

(ii) These phenomena failed to appear during simultaneous treatment with INH and streptomycin. In the lymph nodes, merely a diffuse lymphoid hyperplasia was seen at this stage of latency.

(iii) During treatment of fully developed tuberculosis (especially with INH), cells of the transitional type, immature plasmablasts predominate and active lymph follicles are more numerous. Plasmacellular reaction and follicle activity are more marked than in the early control groups.

(iv) Regressive changes are accompanied by mature plasmacellular reaction in the lymph nodes. In contrast to earlier statements, encapsulation and absorption of caseous foci were in our experiments invariably attended by the presence of plasma cells around the focus, in the fibrous capsule, or at the margin of the caseous matter.

In a few animals productive tuberculosis developed. It was in these animals that the most marked plasmacellular reaction occurred.

The reactions mentioned did not appear in the periportal mesenteric lymph nodes.

The changes in the spleen were similar to those of the lymph nodes, they occurred, however, at a later time (haematogenous origin).

Toxic doses of INH resulted in severe changes in the entire lymph apparatus. Cell damage was most marked in plasma cells which in some cases underwent complete destruction.

If INH and streptomycin were administered to healthy animals for three months, no tissue reaction like the above did take place. Physiological differences between the individual lymph nodes were rather indistinct and diffuse lymphoid hyperplasia prevailed.

In the animals treated with therapeutic doses of INH follicular haemorrhages destroying the germinative centre were observed.

Acute Diffuse Endangitis of Leptomeningeal Vessels in Landouzy's Typhobacillosis

J. Juhász

(1st Dept. of Pathological Anatomy, Medical University, Budapest)

Vessel changes occurring with tuberculous meningitis are markedly influenced by streptomycin therapy. Since the advent of this antibiotic, uninfluenced vessel, changes associated with tuberculous meningitis are rarely observed. — In the patient reported, a man 75 years of age, the opening of a cervical tuberculous lymph node abscess was followed 3 weeks later by fever, enlargement of spleen and liver, and grave general condition. The patient died one month later. Necropsy revealed tuberculous abscesses in the cervical, thoracal, abdominal, and inguinal lymph nodes, further miliary necroses in the spleen, liver, lungs, and kidneys, and some hardly visible exudation on the brain basis.

Histology has shown that each tubercle consisted of a necrotic focus full of acid fast bacteria, without any proliferative reaction. The exudate on the brain basis contained fibrin, leucocytes, and lymphocytes. Tubercles have not developed at this place either. In the small arteries below the intima there were exudation foci made up of leucocytes, lymphocytes and large

polygonal cells with a foamy cytoplasm. The foci showed a circular arrangement and detached the intima from its basis. The media was most frequently intact. No fibroblasts or hyaline changes were present in the subintimal exudate.

These vessel changes differ from those found in tuberculous meningitis. Their development was presumably due to the age of the patient and his immunobiologic state.

Tuberculous Meningo-Encephalitis

Gy. Róna

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The exudate or granulation tissue of tuberculous meningitis may invade the brain substance in untreated acute cases. This process is termed tuberculous meningoencephalitis. Since the advent of antibiotics the process has become more frequent, because the course of the disease is longer. In 114 of 200 examined cases (57 per cent) the invasion was observed on gross examination. In 100 cases in which INH or streptomycin had been administered for at least 6 weeks, the lesion of the brain substance was invariably present. Initially, the capillaries of the cortex are in the vicinity of the exudate, greatly dilated. Later, the exudate and granulation tissue extends along the vessels, into the cortex, and gives rise to emollition foci. In severe cases characterized by vessel alterations, the brain substance may sequestrate. Within the sequestrated part there may remain comparatively intact brain islets. On the border of the liquefied area fat-laden cells or gliosis may occur. Later, the specific character of granulations, both on the meninges and in the brain substance gradually disappears and fat-laden cells, fibroblasts, and giant cells larger than the Langhans type, prevail. *Gömöri's* stain shows that the damaged brain parts have been invaded by many new capillaries surrounded by lymphocytes and plasma cells. Glia tissue passes into the brain along the vessels.

Besides the areas neighbouring the exudate masses, brain lesions occur also in parts covered with intact meninges, further far from them, even in the basal ganglia. Perivascular round cell infiltrations and demyelinisation, central dissolution of the tigroid, its cloddy transformation and disappearance may be observed.

After the acute process has subsided the amount of fibrous glia increases. Small emollition foci are replaced by star-shaped glia scars, and diffuse gliosis shows in the environment full of shrunken ganglion cells.

These examinations demonstrate that tuberculous meningitis is, owing to its prolonged course, always a meningoencephalitis. The brain process is close by associated with the meningeal one and may, after meningeal restitution, become prevalent both clinically and anatomic-histologically. This kind of brain lesion represents, beside the emollitions due to vessel changes and the tubercles of the parenchyma, the most important problem of tuberculous meningitis,

Endocrine Organs in Tuberculosis. — Correlation of the Endocrine Apparatus and Haemorrhagic Diathesis in Tuberculous Patients

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There is an imbalance of the epiphyseo-hypophyseal system in tuberculous patients. showing itself in a morphologically demonstrable shift in favour of the adenohypophysis. The increased sexual libido of tuberculous subjects may be due to this endocrine change. — Another endocrine change in tuberculosis is adrenal hypoplasia. The tendency to bleeding is under endocrine control, in which a prominent role is played by the adrenal cortex. In women, the tendency to bleeding due to disturbances of the hypothalamic centre and the adrenal cortex and to changes in the corpus luteum, may occur on a familial hereditary basis. This entity has been termed endocrine haemorrhagic diathesis by the lecturer. In men, haemorrhagic diathesis is prevented by the hypothalamo-adrenal system, whilst in women there is a double defensive mechanism, consisting of the hypothalamus, the hypophyseal centre and the corpus luteum.

Boeck's Sarcoid and Tuberculosis

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Several cases of *Boeck's* sarcoid are reported, two have been examined post mortem. Three cases deserve attention from the point of view of distinguishing Boeck's sarcoid from tuberculosis.

1. A man, 58 years of age had suffered for 10 years from a gradual atrophy of his limbs. With muscle biopsy, tuberculous granulation tissue and acid fast bacilli were found. The diagnosis of tuberculous myositis was established. 3 years later he died of the sequels of nephrolithiasis. Necropsy and histology revealed typical Boeck's sarcoid in the mediastinal lymph nodes. 2. In a girl 6 years of age enlargement of the liver and spleen, *Mikulitz'* syndrome, swelling of the mediastinal and peripheral lymph nodes, and skin symptoms were present. An axillary conglomerate was removed and examined for tuberculosis. Histology revealed *Boeck's* sarcoid. 3. A 26 years old man had been treated for tuberculous bronchoadenitis and epididymytis in 1949. In 1953 he developed generalized enlargement of the lymph nodes. On the basis of histology, this disease, too, was believed to be of tuberculous origin and the patient was treated with streptomycin, isonicotinic acid hydrazide, and PAS, for 7 months. Treatment was unsuccessful. Histological control carried out in our institute revealed Boeck's sarcoid.

With respect to the divergent literary data concerning the relationship of tuberculosis and Boeck's sarcoid, attention is called to the fact that differential diagnosis should be based on the evaluation of all factors, viz. clinical data, histology, bacteriology, and the efficiency of specific therapy.

A Case of Myocardial Tuberculosis

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In the reported very rare case, numerous disseminated tubercles were found in the myocardium. The male patient 68 years of age, was being treated for heart complaints. The ECG was not characteristic, it pointed to conduction disorder and coronary insufficiency. Necropsy revealed extensive tuberculosis of the heart musculature, whereas the coronary arteries displayed little morbid change. With regard to the highly effective drugs against tuberculosis, the condition may be curable if diagnosed during life. Decompensation occurring in a patient suffering from tuberculosis may raise the suspicion that the myocardium has been involved in the specific process.

Histology of Tuberculous Empyema

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Extirpation of the sac of the empyema is carried out with increasing frequency in modern surgical treatment of tuberculosis. Tissues removed at operation were histologically worked up. The visceral pleura, the parietal pleura, and the sinuses were separately examined. Special attention was paid to eventual fistulas. These were separately worked up together with their environment. In accordance with literary data, tuberculous changes were found in both layers of the pleura, nearly invariably in the parietal layer and rather frequently in the visceral one. The environment of a fistula always contains specific granulation tissue. The conclusion is drawn from these facts that extirpation of the empyema sac is useful, since it contains, within a massive scar impermeable to drugs, infectious specific matter which, being inaccessible to therapy, represents a constant danger for the organism. If the empyema sac is left in place, a well defended tuberculous focus remains in the organism, occasionally giving rise to relapses or dissemination.

Histology of the Pleura Removed at Decortication and Lung Resection for Tuberculosis

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The pleura removed at operation of 102 patients was examined in order to compare the changes found with the course of the disease. The visceral pleura was less involved by inflammation than the parietal layer. The scar coat of the former was thinner and contained a lesser number of vessels. Inflammatory infiltration and tubercles were more frequent in the parietal pleura. These facts follow from anatomic and absorption conditions, since absorption from the pleural cavity takes place mainly through the parietal layer.

Pleural changes have been classified as follows : (i) Callus, with little, or no, inflammatory changes. It is chiefly the sequel of pneumothorax therapy. The basic condition was often a tuberculoma. (ii) Pseudoempyema. This is a chronic, fibrinous-callous pleuritis in which the exudate turns into a homogeneous, eosinophilic mass *(Pagel and Wurm)*. Little specific change is found on histology. This form may also result from previous caseous pleuritis. (iii) Aspecific empyema, not associated with formation of tubercles in the callus (irrespective of the result of bacteriological examination). (iv) Specific empyema associated with the formation of specific granulation tissue in the callus, like in the wall of a tuberculous cavity.

On the basis of this classification it has been concluded that in the material worked up the pleural changes recorded were closely related to the basic pulmonary process and collapse therapy. Clinical diagnosis anf the result of histologic examination are often divergent.

Paraspecific Lymph Node Changes in Phlyctaena

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Enlargement of the lymph nodes in phlyctaena has long been observed. Recently, tuberculosis of the lymph nodes is considered the primary process. The question has been raised whether the lymph nodes are or are not invariably affected with tuberculosis. This is particularly important in cases in which there is no active focus in the lung. — The authors examined the cervical and axillary lymph nodes of patients with phlyctaena admitted to the Dept. of Ophthalmology. These lymph nodes were enlarged in 59 per cent of the examined patients, while the inguinal nodes in 48 per cent. About one third of the lymph nodes were tuberculous. Lymph node changes not displaying tuberculous granulation were termed paraspecific in order to underline the hyperergic character of the changes. The general and paraspecific character of the changes follows further from the fact that they were present also in other lymph nodes of the patients suffering from phlyctaena or another ophthalmologic disease of tuberculous origin. These changes are accordingly held characteristic of some lesion to the organism, in the present of the tuberculous infection, rather than the phlyctaena.

Pathohistology of Renal Tuberculosis

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200 tuberculous kidneys, most of which had been removed at operation, were examined. Aspecific vascular lesions, far from the tuberculous areas, occurred more frequently than specific changes. Among the former, the earliest were swelling of the glomerular endothelium, serous imbibition of the basal membrane, exudation in *Bowman*' s capsule. Later, shrinkage of the tuft beginning at the vessel pole, and, finally, its hyalinization occur over large cortical areas. — In small arteries and arterioles serous imbibition and homogenization of the wall was frequently

observed, especially in the afferent arteriole. The hyaline thickening of the vascular wall results in narrowing of the lumen. In the small arteries there are endarteritis-like changes resembling those in pyelonephritis, except that the elastic fibres do not increase in number. There is cell proliferation and many argentaffine fibres are present.

A thyroid-like structure, similar to the one held characteristic of the 3rd stage of pyelonephritis, may also be met with in renal tuberculosis. Further, extensive aspecific infiltrations resembling the picture of pyelonephritis may be seen.

In the authors' opinion, the aspecific changes are produced by tuberculosis bacteria. It is still unsettled whether they are due to a direct toxic effect or to the allergic state of the organism. Eventual secondary infections are doubtlessly playing a role. The changes discussed should be given due consideration in treatment.

Pathological Relationships of the Tuberculosis of Female Genital Organs

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74 cases of female genital tuberculosis were analysed. In no cases was there suspicion of tuberculosis, diagnosis was in all cases established from biopsy material. (i) In 33 cases the Fallopian tubes and ovaries were affected. (ii) Curettage carried out for sterility or amenorrhoea (ovarial dysfunction) results in the diagnosis of endometrial tuberculosis with an increasing frequency. Sterility and amenorrhoea are very often due to destruction of the endometrium by the specific process. (iii) Tuberculous myometritis is a rare incidence. It was found in three of 74 cases. In one of them the myometrium alone was affected. (iv) Tuberculosis of the portion is rather infrequent. The number of such cases will probably increase with the increasing application of biopsy. Out of 74 patients tuberculosis of the portion occurred in 5, and in 2 of the latter cancer (squamous cell carcinoma) was also revealed. — Beside these, a rare localization of tuberculosis, that of the Bartholinian glands, should be mentioned. This process is very likely due to inoculation. The unexpected diagnosis of genital tuberculosis has its own importance in public health, since in this way more cases of latent tuberculosis become accessible to treatment.

Tuberculosis of the External Genital Organs, with Special Regard to Intracanalicular Spreading

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In the last 10 years, 1.43 per cent of the patients admitted to the department suffered from genital tuberculosis (190 patients). Tuberculosis of the cervix and portion occurred in 11, that of the vagina in 1 and that of the vulva in 1 cases. Analysis of the material has shown that haematogenous spread is less frequent than intracanalicular one passing from the peritoneum through the tubes to the endometrium. Pleural and peritoneal exudates were often mentioned in the history. Special attention is called to the fact that the lower end of the genital canal (inner orifice) is rarely affected in comparison with the tubes. The mucosa of the tubes represents, under physiological conditions and in case of ascites, a wide absorption surface, upon which bacteria easily concentrate. Intracanalicular spreading may often be demonstrated by examining serial sections. The mechanism of spread should all the more be learned, as the mode of prevention could be devised in this way. Women suffering from pleural or peritioneal exudates should, especially at the age of puberty, be given particular protection, their genital affections and complaints must be treated with great care. It is with their special absorbing capacity rather than with some affinity to tuberculosis of the individual mucosal surfaces (tubes, endometrium, cervix), that the single parts of the genital organs differ from each other. It is for this reason that the endocervix seems to be protected. The diagnosis of isolated tuberculosis of the portion and of the cervix must always be considered with scepticism, affection of the upper sections being almost invariably present. A case of vulvar tuberculosis leading to elephantiasis deserves to be mentioned both because its rarity and implications in differential diagnosis.

Tuberculous Endometritis

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Tuberculous endometritis was revealed in our material in 38 cases during 7 years. The total number of samples obtained at curettage was 5105, the percentage of endometrial tuberculosis was 0.74. On the basis of these examinations and some necropsies revealing genital tuberculosis, the pathogenesis, histomorphology and the correlations of genital and pulmonary tuberculosis are discussed. Specific therapy was in some cases successful, as seen from the control examination of the endometrium. The age of the patients was between 21 and 40 years. Their majority was examined for irregular bleeding, whilst sterility was a less frequent cause of the examination.

Tuberculous Otitis in Infancy

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Tuberculous otitis is infrequent in infants. It is characterized by a latent onset, a protracted and torpid course, seromucinous exudate, a greyish yellow drum, and the slow development of mastoideal changes. These manifest themselves as necrotizing mastoiditis, fibrocaseous osteomyelitis, or tuberculosis in the sinus *(Germán.)* 3 cases are presented. The first one has been operated on for mastoiditis attended by meningism. Necrosis and greyish-pink granulations were found in the mastoid, the major part of the tegmen was destroyed, there were tubercles on the dura. Combined antibiotic treatment resulted in restoration. In the bone fragments of tubercles were revealed. In 2 other cases no operation had been performed and the mastoid was examined only at necropsy. Bone destruction and typical tuberculous granulation tissue, partly with central caseation, were found.

Pathology of Tuberculous Spondylitis

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The neurosurgical significance of tuberculous spondylitis depends on the appearance of spinal cord symptoms. 87 cases with spinal cord complications were observed. The conclusion was drawn that the neurologic symptoms are due to the specific process extending to the intervertebral structures, since only these may account for symptoms due to compression. Processes localized in the vertebral body do not give rise to clinical symptoms before spreading to the intervertebral structures. Subsequently, when the process has reached the disk, specific granulation tissue, a sequester, a destroyed or herniated disk, or an abscess may compress the spinal cord. An isolated focus in the vertebral body does not give rise to symptoms. The extension of the process from the vertebral body towards the disk depends on physical factors acting upon the spine. As a rule, the static disorders of the spine (luxation, angle formation) are also due to changes in the disk apparatus. The disk being nourished by diffusion only i. e. by a process depending on the intactness of the corpus, it is warranted to assume that changes involving the body of the vertebra are soon followed by degeneration of the disk. This is often the first sign of spondylitis which, at the same time, may promote the extension of the specific process to the intervertebral structures and into the spinal canal.

Crohn's Disease, with Special Regard to its Localization and Differentiation from Tuberculosis

Anna Sztanojevits, J. Ormos

(Dept. of Pathological Anatomy, Medical University, Szeged)

5 cases are reported, 3 of them occurred in the colon so that it was more appropriate to apply to the process the term *Crohn*'s disease instead of terminal ileitis. In the cases examined changes were present, beside those of the bowels, also in the liver and the spleen. The latter should be sharply differentiated from tuberculous changes of the same organs. The lymph vessels are invariably involved so that elephantiasis of the intestinal wall may develop, with progression of the disease the characteristic histological changes gradually disappear and diagnosis becomes difficult.

SECTIONAL MEETING

I. Forensic Medicine

Acute Lethal Colchicine Poisoning

Gy. Farkas

(Dept. of Forensic Medicine, Medical University, Pécs)

A 30 years old man ingested, by mistaking the compound for another drug, a lethal dose of colchicine. Clinical symptoms, necropsy and histologic findings, were similar to those found in animal experiments.

Conditional Reflex and Working Capacity of Subjects Without Hands

K. Beöthy

(Dept. of Forensic Medicine, Medical University, Pécs)

2 patients are demonstrated and the mode of developing conditional reflexes, their importance, transformation to unconditional reflexes, with special regard to the ability of working are discussed. The present procedures of establishing the percentage of inability are unmaintainable. Finally, the problems of complex functional therapy and rehabilitation schools are mentioned.

The Opening of Alveoli in the Foetus on Experimental Putrefaction

S. Ökrös

(Dept. of Forensic Medicine, Medical University, Debrecen)

Experimental putrefaction of macerated mature foetuses was performed by keeping them in the open air, or buried in the ground. Atelectasic foetal lungs were, where the air passages had been closed by a solid substance (earth, water, detritus), kept in water for 6 to 14 days. The tension exerted by gases of putrid processes gave rise to the opening of alveoli in a part of the lobule, the entire lobule, or in lobule groups, whereby the lung imitated the picture produced by respiration. In the atelectasic lungs of mature foetuses the alveoli give way to the gases at a pressure as low as a few mm mercury. A pressure of 20 mm Hg results in the opening of all alveoli,

and at a pressure of 50 mm they become distended. Rupture of marginal alveoli in situ takes place at a pressure of 90 mm while in the removed lung at 60 mm. Then air enters into the interlobular tissue and, finally, the pleura also ruptures. Putrid processes produce so much gas as suffices to open the alveoli. In putrefied foetuses the fact that opened alveoli are present admits no conclusion as to viability. On stating viability or stillbirth other evidence too must be taken into consideration.

Brain Changes after Temporary Survival of Hanging

L. Dános

(Dept. of Forensic Medicine, Medical University, Pécs)

A man 41 years of age lived 55 hours after he had hanged himself. Strangulation lasted for 5 minutes. Aside from the comparative intactness of the occipital cortex, signs of extensive anoxia were present.

Experimental Data Pertinent to the Results Obtainable by Exhumation

K. Kerekes

(Dept. of Forensic Medicine, Medical University, Pécs)

The experiments aimed at establishing how long pathogenic agents in the buried dead body preserve their pathogeneticity in dependence on the quality of the ground, and other factors, such as the temperature. The data can be evaluated in exhumations. (Pathogenicity was judged from culture results.)

Effect of Water Pressure on the Passage of Fluid into the Air Ways after Death

Gy. Incze, J. Gyöngyösi

(Dept. of Forensic Medicine, Medical University, Budapest)

It had been established previously that natural motions of water (wave, stream) may result in that water and the particles suspended in it flow into the air ways of the dead body floating on the surface, and occasionally pass as far as to the subpleural spaces. In recent experiments it has been found that, admitting the dead body is under the water surface, the pressure of water suffices to allow water and particles to attain the subpleural lung area.

Bone Marrow and Bone Tissue Embolism as a Vital Reaction

Gy. Incze, A. Árvay

(Dept. of Forensic Medicine, Medical University, Budapest)

In previous examinations it had been found that, following forced death associated with bone injury, bone marrow emboli and minute boneparticles appear in the right half of the heart and the branches of the pulmonary artery. It had been claimed that this kind of embolism may, unlike other embolisms due to injury, serve even long after death to prove that the bone lesion has occurred during life. The examinations have proved that from the microscopic bone splinter found in the veins draining the area of bone injury it becomes possible to determine from which bone, or bones, of the organism the splinter had been detached.

The Time of Appearance of Agglutinin Properties

R. Budvári

(Dept. of Forensic Medicine, Medical University, Budapest)

Agglutinin properties are not developed simultaneously with agglutinogen properties, but, as a rule, only after birth. Therefore, blood typing may present difficulties before the end of the 6th month. Knowing the problem of»serological maturation«, the court of justice often asks the expert's opinion on the reliability of typing performed for establishing paternity. To answer such questions, statistical tables have been constructed by the author on the basis of data derived from a vast infant material, in order to show time of partial or full appearance of agglutinins. No other data based on a similarly large material has as yet been published. On the basis of this table the results of typing of infants can be evaluated with ease.

Meteoropathologic Relationships of Sudden Death

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On the basis of 1000 cases examined post mortem, the correlation on front changes and the time of sudden death was studied. In all cases, the morbid condition giving rise to death was also taken into consideration. It has been shown that cases of sudden death cumulate at the time of front changes. Statistical evaluation of the results prints to the biologic activity of fronts.

Acute Changes in the Conduction System in Cases of Sudden Death from Heart Failure

A. Árvay, O. Szücs

(Dept. of Forensic Medicine, Medical University, Budapest)

The conduction system was examined in serial sections in cases where the heart showed no fresh lesions accounting for the sudden death either grossly or microscopically. In part of the cases changes were found in the node of Aschoff—Tawara, bundle of His and the initial sections of the branches, which, according to clinical, pathological and experimental observations, might have induced ventricular fibrillation and sudden heart failure.

Spontaneous Rupture of the Heart in a 4 Month Old Infant

L. Dános

(Dept. of Forensic Medicine, Medical University, Pécs)

The spontaneous rupture was due to a developmental anomaly of the heart apex. The case was reported on account of its rarity.

Death due to Cerebral Lesions in the Newborn and During Later Infancy. Relationships of these Deaths to Fatal Aspiration

Gy. Farkas

(Dept. of Forensic Medicine, Medical University, Pécs)

At the necropsy of infants died in consequence of aspiration, cerebral lesions were frequently found on gross or microscopic examination. Thus, aspiration has little to do with overfeeding, improper management, or disturbed motility of the stomach ; it is due to cerebral, occasionally inflammatory, lesions. In such cases the designation of the disease girm as the cause of death should be modified.

Lung Changes in Infants after Sudden Death

E. Somogyi

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Following sudden death of infants, necropsy may reveal numerous morbid changes ranging from bronchiolitis to the various types of pneumonia. The pathological processes develop in a short time and associate themselves, owing to the comparative underdevelopment of the infantile lung, with hypoxia, deteriorated circulation, consequential changes in the nervous system, and metabolic disorders, readily leading to sudden death.

The Concentration of Ether in the Blood and the Organs Following Administration of an Overdose of Ether in Man and in Animals

I. Gy. Fazekas, B. Rengei, F. Harmath, J. Kirai

(Dept. of Forensic Medicine, Szeged)

The concentration of ether in the blood and in various organs has been determined by the Widmark-method in rabbits, guinea pigs, rats, mice and cats following death induced by an overdose of ether. The values so obtained were then compared with similar data for two subjects who had died during ether anaesthesia. The lowest lethal blood level of ether is almost identical in man, in the dog, cat, rabbit and rat ; in the guinea pig and in mice it is higher than in man. The blood in the left heart usually contained somewhat more ether than blood in the right heart or in the peripheral veins. The ether content of parenchymatous organs was higher than, and that of the brain almost identical with, that of the blood in the left heart. The conclusion is drawn that exact determination of the lowest blood level of ether lethal for man requires further investigations.

Simultaneous Quantitative Determination of Ether and Alcohol in Tissue Fluids

J. Nagy, Márta Dézsi, L. Lóczi

(Dept. of Forensic Medicine, Medical University, Debrecen)

To determine ether and alcohol simultaneously in blood, *Widmark*'s and *Nagy*'s methods were employed, then the result of *Nagy*'s method was sustracted from that obtained by *Widmark*'s procedure. The difference represents the ether contents ; the method of *Widmark* yielding the sum of ether and alcohol, that of *Nagy* the alcohol contents only. The result of subtraction must be multiplied with the factor 0.8142, the quotient of the factors of sodium bichromate referred to alcohol, and ether, respectively.

Further Examinations of the Effect of Alcohol on Hearing Capacity

Á. Kósa

(Dept. of Forensic Medicine, Medical University, Debrecen)

The effect of alcohol on hearing was examined in humans. Volunteers were given to drink, in the form of rum, 1 ml of concentrated alcohol per kg of body weight. Audiometry was performed 1, 2 and 3 hours after the intake of the fluid. By the end of the 2nd hour, hearing deterioration was from 15 to 20 dB in alcohol addicts, whilst those not addicted to alcohol displayed a decrease of hearing of 5 to 10 dB only, when examined with the tone pitches from c_5 to c_7. The differences are significant. On this ground, the hearing curve taken after alcohol consumption will show whether or not the experimental subject has been an alcohol consumer.

Effect of Low Doses of Alcohol on the Capacity of Driving a Motor Vehicle

J. Gyöngyösi, L. Horváth

(Dept. of Forensic Medicine, Medical University, Budapest)

100 examinations have shown that the intake of amounts of alcohol so small (40 g) as giving rise to no clinical sign demonstrable by physical methods, the impairment of driving capacity can still be demonstrated by means of electric measuring apparatuses. (1) In more than 60 per cent of the examined persons the perception time of all important colours, including white, was found prolonged. The prolongation was more marked in alcohol addicts. (2) In non-consumers of alcohol the percentage of mistakes increased in 67.5 per cent, thus traffic security decreases. (3) Though the percentage of mistakes of alcohol consumers decreased in comparison to what had been found prior to intake of the above dose, it was, despite the improvement, still considerably higher than that of the non-consumers after intake of alcohol.

The Effect of Chronic Lead and Alcohol Poisoning on the Skeletal Muscles of Small Animals

Z. Szabó

(Dept. of Forensic Medicine, Medical University, Debrecen)

Comparative toxicologic studies were carried out in white rats exposed to chronic poisoning with lead, alcohol, and broth. The control animals were given the same volume of physiological salt solution. The effect of poisoning was determined by the examination of muscle power (compulsory climbing), further the changes in weight were recorded, and sections of nerves were examined after supravital staining with methylene blue. The most severe alterations occurred in the group treated with lead *and* alcohol. Thus, the poisoning effect of lead is rendered more severe by alcohol.

Experiments with the Absorption of Alcoholic Beverages Containing a Certain Amount, or No Carbon Dioxide

Gy. Farkas

(Dept. of Forensic Medicine, Medical University, Pécs)

The examinations performed with *Widmark*'s method resulted in the well known fact that fluids containing alcohol and carbon dioxide are absorbed at a higher rate than those made without carbon dioxide. Therefore, of alcoholic fluids containing carbon dioxide smaller Quantities suffice to produce an alcohol concentration in the blood (as interfering with psychic quanfities suffice to produce an alcohol concentration in the blood) as interfering with psychic functions.

SECTIONAL MEETING

II. Morphological Subjects

Functional Structure of Tendon Sulci

G. Balogh, I. Földes

(Dept. of Anatomy, Medical University, Debrecen)

The effect of mechanical factors on the structure of tendon grooves was examined in the sulcus retromalleolaris lateralis, sulcus retromalleolaris medialis, sulcus musc. peronei longi, sulcus hamuli pterygoidei, sulcus intertubercularis, incisura ischiadica minor, and the sulcus musc. flexoris hallucis longi. Results : (i) At the upper section of the retromalleolar lateralis sulcus, where the tendon exerts no mechanical action and only passes along the bone, no cartilage is present. — (ii) The other examined grooves are covered with cartilage which exhibits, according to the stimulus, a lamellar structure. The surface consists of collageneous fibrous cartilage, corresponding to the pressure and scissor effect acting there, whilst the counter-pressure effect acting directly on the bone has led to formation of hyaline cartilage. — (iii) Certain changes occur with age. In the old, the so-called transitional cartilagineous layer is considerably broader, owing to functional influences. — (iv) The strength of the mechanical effect exerts an influence on the thickness of the developing cartilage. — (v) Prior to the evolution of the cartilage, obliteration of capillaries takes place. This process is probably in relation with the evolution of cartilage.

Roentgen-Anatomic Studies on the Lumbar Spine of Sportsmen in Extreme Positions

P. Lajkó, M. Nemessuri

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Despite the extensive application of X-rays, little attention has been paid to the morphologic analysis of the extreme positions of the spinal column. The recognition of morbid conditions is, however impossible before the normal ones are established. Therefore, the single parts of the spine of healthy subjects were examined in extreme positions, such as bending forward, backward, and to the side, rotation, and the »bridge« position. Difficulties were met in regard of the mode of examination, and the numerical expression of the motions. It is inferred from the examinations that the greater flexibility of the lumbar spine in sportsmen is a sign of an increased general capacity to adaptate. The data collected should be completed with those of various age groups in order to create a basis for evaluating findings obtained in pathological conditions.

Development of the Oesophageal Epithelium under Normal and Experimental Conditions

A. Barcsa, L. Mohácsi

(Dept. of Anatomy, Medical University, Debrecen)

The development of the oesophagus was examined in chicken from the 3rd day of the incubation of the egg until the first feeding and the effect of this function upon the developed organ was observed. The effect of food of various physical properties, further that of feeding

through a tube, when nothing was swallowed, were studied. On the 9th day, when the first swallowing movements began and the circular muscles appeared, the whole structure of the organ, especially its epithelium, underwent considerable changes. The next great change occurred at the beginning of independent nutrition, when the final structure is evolved according to the quality of the food. The muscle coat becomes stronger, the epithelium flattened and depending on the food, of various thickness. The picture of such normal gullets represents an interesting contrast to that of the chicken fed through a tube. — It was concluded from the examinations that functions exert a considerable effect on the formation of the structure of organs, the organism being compelled to respond to external stimuli with adequate reactions.

Experimental Angioplasty with Lyophilized Vessels

Gy. Bornemissza, I. Szilágyi, G. Bakó, Antónia Kiss, Valéria Ressmann, F. Tóth

(Dept. of Surgical Anatomy and Operative Surgery, Medical University, Debrecen)

The biologic problems of vessel homoiotransplantation, with special regard to the methods of conservation and storage are discussed. — A procedure consisting in the lyophilization of vessels has been devised. The sterile vessel piece is cooled under carbon dioxide snow to —80° C, then dried in vacuum. The fine ice granules brought about by quick cooling do not damage the tissues and in the vacuum undergo sublimation. The vessel pieces kept under vacuum in sealed tubes can be stored at room temperature, they need no cooling apparatus, and may easily be transported. The method will help to solve some of the biologic problems of homoiotransplantation. Successful transplantation could be carried out with vessels stored for 6 weeks, and it is hoped that vessels may be stored in this manner even for a longer time.

The Post-stenotic Dilatation of Great Vessels

F. Robicsek

(Postgraduate School of Surgery, Medical University, Budapest)

The post-stenotic dilatation of the great vessels is a not infrequent occurrence, for which we were unable to find a satisfactory explanation in the literature. On basis of hydrodynamical experiments, clinical observations and histological examinations made by the author revealed that in the development of a post-stenotic dilatation the turbulent flow injuring the elastic elements of the vascular wall plays an important etiological role.

Morphology of Pacchionian Bodies

F. Kiss, J. Sattler

(Dept. of Anatomy, Medical University, Budapest)

Pacchionian bodies are found not only in adults, but in a primitive form, also in infants. Between their connective tissue-bundles there is a breach system connected, with the subarachnoidal CSF through the main canal running in the pedicle. The surface of the Pacchionian body is enclosed in a fibrous capsule (perigranular capsule) formed by the dura. The space between the capsule and the Pacchionian body communicates with the subdural space. In the bodies nerves and terminal apparatuses have been found. Site and structure of the bodies is nearly identical with those of the sinus organ of fishes. The latter organ too is situated between two fluids of different pressure (CSF and endolymph). Our examinations have not ascertained any of the theories referring to the function of the bodies, but they favour the assumption that a pressure measuring interoceptor, a baroceptor is dealt with. In some of the bodies islets made up of epitheloid cells have been detected. The cells of the islets differ from the other elements

of the body in regard of shape and staining reactions. According to their morphology, the islets are similar to the areas of Langerhans in the pancreas. They probably exert an endocrine function, their product passing into the CSF. Experimental examinations of the islets are being continued.

Demonstration of Plexus Myentericus Auerbachi and Plexus Submucosus Meissneri Silver Impregnated Specimens

S. Kalapos

(Dept. of Anatomy, Medical University, Debrecen)

Demonstration of both plexuses, on full plane sections including the distinction of the meshwork of lst order from that of 2nd order. The various forms of nerve cells occurring in different sections of the digestive traet are shown.

Histology of the Interstitial Ground Substance with Special Regard to the Central Nervous System

G. Kelényi

(Dept. of Pathological Anatomy, Medical University, Pécs)

The elements binding colloid iron, and their affinity to this substance, have been studied, constantly controlling electrometrically the pH. In this respect there are marked differences in the negativity of the various structures. Changes occurring on digestion in the interstitial groudn substance and in the various structures were studied. It is emphasized that within the grey matter of the central nervous system there is a well developed ground substance which has not been given due attention. Under pathologic conditions changes may occur in this substance.

Innervation of the Mesenterial Lymph Vessels

I. Kubik, J. Szabó

(Dept. of Anatomy, Medical University, Budapest)

Up to now morphologic examination of lymph vessels has been limited to those of the thoracic duct and the spermatic cord. Apart from *Zhdanov* who examined the thoracid duct after silver impregnation, supravital methylene blue has been employed.

In the present examinations *Gross—Schultze*'s impregnation technique was applied to the mesenteric lymph vessels of the cat. For comparison, Nagy's supravital methylene blue method was used.

The following could be established. (i) Similarly to blood vessels, lymph vessels are accompanied by thicker nerve bundles twisting around the vessel. As a rule, the lymph vessel does not receive branches from them. (ii) The fibres passing to the lymph vessels reach them together with the capillaries, or originate from a nerve bundle running at a distance from the vessel. (iii) On a part of the vessels a typical »Grundplexus« occurs. (iv) Most vessels have a plexus innervation, the fibres forming a plexus surrounding the vessel like a meshwork. Most of these fibres are probably of sensory nature, as indicated by their thickness and their degeneration after extirpation of the spinal ganglia. (v) Characteristic end apparatuses of the *Vater-Paccini* type adhere to the lymph vessels, encircling them in the form of a fork or a hook.

Further examinations will have to determine the functional distribution of the elements constituting the plexuses. The fact that among the nerves of the lymph vessels afferent elements occur in a great number allows some conclusions as to an adaptation mechanism which we already succeeded in demonstrating in the thoracic duct and the major lymph vessels.

Examination of Nerve Regeneration in the Rat's Skin

I. Dévényi, J. Nagy

(Dept. of Pathological Anatomy and Dept. of Forensic Medicine, Medical University, Debrecen)

The regeneration of nerve elements was examined in skin wounds on the back of rats. Silver impregnation *(Troitsky's* block method) and supravital methylene blue staining were employed (in *Nagy*'s modification).

As early as on the 5th day, nerve elements appear simultaneously with the granulation tissue. They originate partly from nerves of the intact environment, partly from those accompanying the vessels in the granulation tissue.

With respect to the quality of fibres the period of examination, which lasted for from 1 to 65 days, could be divided in three phases. Between the lst and 18th days the fibres are swollen, they stain unevenly, no myelin sheath is present. During the 18th—36th days the majority of nerve fibres are still swollen, their stain is more even, some fibres have a medullary sheath. In the 3rd phase lasting from the 37th to the 65th day the majority of fibres are like the intact ones, some of them are, however, swollen, stain unevenly, and undergo destruction at places. Thus the nerve structure of a scar is not yet normal even as late as on the 65th day of wound healing.

Differences could be observed only in preparations stained with methylene blue. Impregnation did not reveal qualitative differences.

Meningitis due to Cryptococcus Neoformans (Torula Histolytica) in Hungary

Anna Csillag, B. Horányi

(State Hygienic Institute, State Institute of Neurology and Psychiatry, Budapest)

A 42 years old woman suffered four relapses of meningo encephalitis in two years (with meningeal symptoms, pyramid signs, central paresis of the hypoglossus nerve, high cell count in the CSF). During the 4th relapse 1100 lymphocytes per cu. mm. were found in the CSF. Meningoencephalitis due to Cryptococcus neoformans was suspected after excluding all possible agents. Cryptococcus was revealed in, and cultivated from, the CSF. Intracerebral administration of the CSF to mice resulted in typical meningoencephalitis, a gelatinous cyst was present on the brain basis, and cryptococci were demonstrated in the brain substance. After the death of the patient, extensive chronic infiltration foci made up of lymphocytes and histiocytes were found on the meninges, and, though smaller ones, within the parenchyma, especially in the area of the medulla oblongata and the spinal cord. In the sections made of these parts Cryptococcus was found. The agent occurred, however, in a strikingly low number in comparison with the gravity of the clinical course and the infiltrations. In the long paravertebral muscles there occurred in the lumbar section a circumscribed granuloma consisting of lymphocytes and fibroblasts. In this granuloma no Cryptococcis have been found.

Changes in the Sympathetic Ganglia in Old Age

Gy. Botár

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The symphathetic ganglia, first of all the coeliac ganglion, were examined in subjects who had died suddenly after the 8th decade with the diagnosis of senile dementia. Bielschowsky-Gross' silver impregnation method, further other methods, qualitative and quantitative, were employed. No young or developing cells have been found in the ganglia. The number of intact cells was as low as 7 per cent. Over 93 per cent of the cells exhibited morbid changes turning to destruction. Following changes have been observed : granulated sudanophil deposits (32 per

cent), non-sudanophil granules (14 per cent), dysharmony of the processes (8 per cent, presence of all of these changes (24 per cent), cell destruction with extensive phagocytosis (15 per cent). The majority of theses changes is thought to be due to the altered cell metabolism. The cell count is in the healthy 114 per square millimeter; in the examined ganglia merely 99 have been found. The fine intercellular fibres have disappeared, the remainder are wavy, twisting. Similar fibre changes have never been observed with any disease.

Histochemical Studies on Degenerating Nerve Fibres

B. Csillik, Gy. Sávay

(Dept. of Anatomy, Medical University, Szeged)

It had been demonstrated in previous experiments that in nerve fibres with an intact myelin sheath the activity of cholinesterase is limited to the myelin sheath, and no activity is present at Ranvier's nodes. In the present examinations the effect of *Waller*'s secondary degeneration upon cholinesterase activity was investigated by means of the β-naphtylacetate method. — In the first three weeks of degeneration the enzyme activity remains unchanged in the globules deriving from the disintegration of myelin sheath. Subsequently the globules gradually lose their activity. In non-myelinic fibres the enzyme activity is not limited to the surface, but is evenly distributed all over the cross section. In these fibres enzyme activity remains unchanged during two weeks, after this time it disappears gradually.

The mineral metabolism of the nerve fibre being regulated probably by the acetylcholine cholinesterase system, the mineral content oft intact and degenerating nerve fibres was examined by means of spodogrammes. It was found that the ash content of intact fibres was mostly limited to the myelin sheath. In degenerating fibres, ash constituents are contained in the peripheral parts of the myelin globules.

Experimental Demyelination

R. Majnár

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Acid phosphate buffer (pH 6.4, 0.9 weight per cent) was injected into the suboccipital istern of dogs. The first doses were followed by violent excitation, then temporary pareses ccurred, finally (after the 8th to 11th treatment) the paralysis involving initially the posterior, ater the anterior limbs has become persisting, and the animals died. Histologic changes have been revealed mainly in the oblongata and the upper cervical segments. The white matter in this area became spongy, particularly under the leptomeninges. Demyelination involved also the pyramid tract, hence the paralyses.

Histology of Myoclonus Epilepsy

B. Horányi

(State Institute of Neurology and Psychiatry, Budapest)

In a typical sporadic case of myoclonus epilepsy, great numbers of *Lafora*'s bodies were present in the dentate and niger nuclei. In the thalamus and the reticular formation their number was less. The cerebellar cortex, striopallidar system, and the oliva contained but a few of them. Myoclonus corpuscles are, as seen from their histochemical reactions, probably made up of protein, lipoid, and carbohydrate-like substances. Otherwise, their histochemical reactions show differences even within the same corpuscle group, probably owing to differences in age. There

were changes in the nerve and glia cells also in areas where no myoclonus corpuscles were found. Similar corpuscles, inclusions, may accompany other diseases of the nervous system. (In a case of senile dementia observed by the author a body was present in a cell of the vestibular nucleus). Their number is, bowever, considerably lower than in myoclonus epilepsy. Their presence is not a condition of the onset of myoclonus. The latter is likely to occur as a sequel of disturbed function in the dentatothalamo-cortical system. Beside the pyramidal tract, the pallido-reticulo-spinal apparatus may also have a role in the efferentation.

SECTIONAL MEETING

III. Pathology

On the Structure of the Collagen Fibre

Ilona Banga

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According to the general opinion, the collagen fibre with its constituents, the fibril and the protofibril, are made up of a single uniform protein, whilst the intermicellar spaces are filled with mucopolysaccharides. The latter represent the so-called ground substance. According to the studies of the author, the fibre is, however, made up of not one but two different protein components differing in physicochemical, polarization, and enzymologic properties. One of the proteins constituting about 20 per cent of the fibrous substance can be isolated in crystalline form. The crystals are similar to the procollagen crystals of *Orekhovich*, and are soluble in a citrate buffer of pH 4 to 5. The heat contraction temperature of this component is lower than that of the entire fibre. The other substance constituting 80 per cent of the collagen fibre, insoluble in a citrate buffer of pH 4, is incapable of acid swelling, but in a pure state it shows swelling in water. Both substances contain carbohydrates and hexosamine.

Polarimetric Examination of Collagen Fibres

D. Szabó, I. Banga

(1st Dept. of Pathological Anatomy, Medical University, Budapest)

In an earlier report we had discussed the qualitative polarimetry of collagen fibres exposed to various influences. Presently, the results of quantitative (imbibition) examinations are reported. In the studies, collagen fibres isolated from the rat's tail were used. The following results have been obtained.

(i) After treatment with heat or chemical substances, two double refraction phases of different intensity can be observed. — (ii) By means of chemical pretreatment it becomes possible to separate the two phases which show quantitative differences under the polarization microscope. — (iii) The type of the curves plotted from imbibition tests supports the view on the complex composition of collagen fibres. This view is further supported by the fact that the resultant of the curves agrees with the well-known imbibition curve of native collagen fibre.

Submicroscopic Structure of Elastic Fibres

Gy. Romhányi

(Dept. of Pathological Anatomy, Medical University, Pécs)

Examination of elastic fibres with elastase and by means of electron microscopy resulted in new data concerning their chemical structural organization. It has been learned that elastic fibres consist of an inner fibril system embedded in a homogeneous matrix. Elastic fibres are optically isotropic, or a mild positive anisotropy may be observed. On treatment with anilin an

intensely negative double refraction becomes apparent, indicative of an inner fibrillar structure agreeing with the electron microscopic picture. A further analysis of the optic phenomenon allowed to establish the fact that the fibrils in the elastic fibre show a spiral course, and that the structural stability of the fibre is partly supported by the matrix substance. The aniline effect depends on the matrix substance and fails to occur after elastase treatment.

Examination of the Fine Structure of Elastic Fibres in Pathological Conditions

M. Németh-Csóka

(Dept. of Pathological Anatomy, Medical University, Pécs)

In the vascular wall the number of elastic fibres increases at sites where the intima is hyperplastic and also in elastic hyperplasia occurring with elevated blood pressure in small arteries. The usual staining methods (resorcin-fuchsin, orcein) do not give means for differentiating these elastic fibres from the intact ones in the media of the normal aorta. After imbibition with aniline the elastic fibres of intimal hyperplasia show, in contrast with normal ones, a decreased, or no, double refraction in polarized light. Similar polarization phenomena are displayed by the elastic fibres of the vessels in old age. The double refraction ensuing after aniline treatment of normal elastic fibres being a sign of their fibrillar structure, these results admit of the conclusion that the elastic fibres occurring with intimal hyperplasia, or in the arteries of old subjects, have a structure differring from the fibrillary structure of normal elastic fibres the fibrillar arrangement is less distinct, or replaced by an amorphous state. Digestion with elastase also suggests structural changes in these morbid elements.

The Intramolecular Structural Stability of Nucleic Acids Studied by Polarisation Microscopy

K. Jobst, Gy. Romhányi

(Dept. of Pathological Anatomy, Medical University, Pécs)

Nucleic acids are negatively double refractive, due to the transversal lamellar position of nucleotids within the molecule. Desoxynucleic acid treated with hydrochloric acid loses its negative double refraction and becomes mildly positively double refractive. The same phenomenon may be observed *in situ*, on cell nucleic acids following salt dissociation of nucleoproteins. This inversion of the optic behaviour may be explained by the desorientation of the intramolecular position of nucleotid bases.

Cellular Reaction to Polyvinylpyrrolidone in Rats

Gy. Dévai, S. Kovács, E. Kovács, L. Galambos

(2nd Dept. of Pathological Anatomy, Medical University, Budapest, and Army Hygienic Service)

Rats were treated with PVP solutions of various concentration and different molecular weight. The animals were killed at intervals of 6 days and their organs were examined for storage and damaging effect of PVP. The last series was examined 54 days after intraperitoneal administration of the substance. Storage was especially marked in the spleen, less marked in the lungs and kidneys. Furthermore, a constant and considerable plasmacellular reaction unobserved in the control animals, was found in the spleen. In the lungs the increase in number of plasma cells was, though to a lesser extent, also present. The authors believe this reaction to be the immunomorphologic manifestation of the antigenic effect of PVP.

Experimental Burn and Permeability

M. Gábor, I. Szórády, K. Sipos

(Depts. of Pharmacology, Paediatrics and Dermatology, Medical University, Szeged)

Rats ranging in weight from 150 to 200 g were shaven on the back and treated intravenously with trypan blue, 10 mg per 100 g of body weight. Application of heat as low as 58°C resulted in an increase of capillary permeability. Higher temperatures eliciting burns disturbed the examinations. After the 72nd hour no increase in permeability was any more present. Since it was found that the capillaries of the rat vary in reactivity to heat stimuli, a new method has been devised to rule out sources of error resulting from these differences and the heat was applied not for a certain time but until permeability had increased, as shown by the appearance of the dye. The minutes elapsing until the appearance of the dye were determined, and termed permeability index. This index is characteristic of the reactivity of the individual animal.

By means of the permeability index the effect on permeability of drugs can be exactly determined. A heat stimulus is applied to two symmetrical skin areas before and after intraperitoneal administration of the drug in question. The difference between the two indexes is due to the effect of the compound administered. The examined compounds (haematoxylin, pyramidon, calcium chlorides, sodium salicylate, Synopen) exhibited a lowering effect on capillary permeability. The strongest effect was observed with calcium and haematoxylin.

It seems that the antihistaminic property of the administered substances does not play a part in the mechanism of the effect.

Nucleic Acid Metabolism of Liver Transplanted to Chorio-Allantoic Membrane

Magdolna Raditz, Z. Pósalaky, T. Barka

(Dept. of Histology and Embryology, Medical University, Budapest)

Liver taken from chicken embryo, rat embryo, newborn and adult rats, respectively, was transplanted into chick chorio-allantoic membrane. Histochemical examination of the transplantates yielded the following results: 1. The rat liver transplanted on the chorio-allantoic membrane behaves in the same manner as in tissue cultures. Adult liver loses its pyroninophilia within 24 hours nearly completely and undergoes degeneration. In newborn and embryonic livers a marginal zone is developed as early as after 6 hours. In that zone the cells are intact and their pyroninophilia is preserved. Gradually however, this zone too degenerates and in 6 days the transplantate is destroyed. Thus in this case, the disappearance of ribonucleinic acid is an irreversible process.

2. The behaviour of embryonic chick liver is not the same as in tissue cultures. A marginal zone is developed but pyroninophilia is resumed in the whole transplantate and, on the 8th day, the entire transplantate is made up of intact liver tissue readily staining with methylgreen-pyronine. Accordingly, in this case the disappearance of ribonucleinic acid is reversible.

Fate of Spermatozoa in the Uterine Cavity

Z. Pósalaki, Gy. Hajdi

(Dept. of Histology and Embryology, Medical University, Budapest)

Rat spermatozoa were injected into the right uterine horn of white rats. The left horn served as control. Within an hour the spermatozoa pass through the epithelium, but some of them remain in the epithelial cells. After two hours they appear deep in the mucosa, to be present in the muscle coat and even in the parametrium by the end of the 5th hour. After 15 to 20 hours they cannot be distinguished from other cells. Histochemical examination shows that the alkaline phosphatase reaction of the epithelial cell is increased in the first 2 hours after the invasion of spermatozoa. 24 hours later it is in the epithelial cells and the submucosa that an increased phosphatase activity occurs.

Effect of Heparin on Rat Mesoappendix

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(2nd Dept. of Medicine and Dept. of Pathological Anatomy, Medical University, Szeged)

It has been assumed that heparin possesses, beside its thrombosis preventing effect, a capacity of dissolving fresh thrombi. In the mesoappendicular vessels of the rat erythrocyte agglutination was brought about by thermocauterization. After the effect of cauterization had stabilized, heparin was intravenously administered (9 to 20 mg) at certain intervals. Injection of heparin 5 and 10 minutes after cauterization brought about in two thirds of the animals immigration of red corpuscles into the mass, or detachment of others from it, loosening of the mass, or its recanalization. Where the injured vessel was in contact with healthy ones, this process nearly invariably occurred.

It is possible to produce, though less frequently, a similar effect by local application of heparin. Heparin is given 30 minutes after cauterization had no effect. The heparin effect was neutralized by simultaneous administration of protamine sulfate or toluidine blue. Histological examinations have shown that the heparin effect does not take place after a real thrombus has been formed.

Intralienal Autotransplantation of Thyroid and Parathyroid in Thyroidectomized Rats. Histophysiology of the Transplants

B. Korpássy

(Dept. of Pathological Anatomy, Medical University, Szeged)

Following problems may be studied after intralienal antotransplantation of one thyroid lobe and the parathyroid gland in thyroidectomized rats. (I) The fate of the transplants and the course of regeneration. (II) If the thyroxin passing directly into the portal circulation becomes inactivated by the liver, will pituitary changes develop and an excess of thyreotrophic hormone excreted? (III) Will hyperplastic or neoplastic changes occur in the intralienal thyroid, as a reaction to the overproduction of thyreotrophic hormone? (IV) Will the direct passage of thyroxin into the portal circulation result in liver changes resembling those found with Graves disease?

The studies revealed the following facts: In some of the animals hyperplastic changes, and a histologic picture pointing to hyperfunction, occurred in the intralienal thyroid and parathyroid tissue. No tumour has, however, developed even in rats surviving beyond 500 days. In some of the animals enlargement of the pituitary and a microscopic picture as common after partial thyroidectomy developed. The liver exhibited mild changes.

Endocrinologic Relationships of Haemoconcentration

K. Kovács, A. Jakobovits, Margit Dávid, Éva Horváth, D. Bachrach

(Dept. of Pathological Anatomy, Medical University, Szeged)

In earlier experiments it was found that in the rat haemoconcentration due to water deprivation is associated with basophilic hyperplasia in the adenohypophysis, and with an increase in the number of Schiff positive cells. At the same time, phenomena of hyperfunction occur in the adrenals and ovaries.

In the present experiments 112 female rats from the same breed were used. One group received a dry diet adequate in every respect while the other group was treated with follicle hormone, of which 100, 500, and 1000 units, respectively, were administered for 8 or, 16 days. In the latter group water was not restricted. A third group was kept on dry food and received follicle hormone.

The examinations revealed that basophilic hyperplasia and the numerical increase of the cells positively reacting to periodic acid-Schiff can be prevented by folliculin treatment, whilst the morphology of the adrenals has not been influenced. These results suggest that basophilic pituitary hyperplasia following haemoconcentration is a sign of active gonadotrophic function. This assumption has been supported by biologic hormone titrations.

The findings suggest that, at any rate in the rat, both gonadotrophic hormones (FSH, LH) produced by the basophil cells, the numerical increase of which is a sign of gonadotrophic hyperfunction.

Morphology of the Cells of the Adenohypophysis

J. Molnár

(State Railways Hospital, Budapest)

Although by classical histological methods only three cell types can be revealed in the adenohypophysis, there are at least six different hormones produced there. The study of their localization has called for a method rendering further subdivision possible. New staining methods devised to this end have been published by *Romeis*, then *Pearse*, *Gömöri*, and *Halmi*. The authors poisoned experimental animals with lead and porphyrine and determined by Rasmussen's method the number of the various cells in the adenohypophysis. The results allow some conclusions as to the pathomechanism of the endocrinologic changes induced by the above toxic agents.

Effect of Nicotine Poisoning on the Structure of the Adrenal Cortex in the Rat

I. Földes, Cs. Hadházy

No manuscript received.

Vital Staining of Damaged Cells in the Alloxan Diabetic Rat

J. Sugár

(State Institute of Oncology, Budapest)

Formation and destruction of cells are processes which occur simultaneously in the healthy organism, but especially in tumours. The degenerating elements of organs undergoing regressive changes for reasons other than tumour formation were studied after vital staining with Niagara sky blue, trypane blue, and Evans blue. The morbid process studied was the alloxan diabetes of the rat, a condition in which beside the beta cells of the islets, the liver and the kidneys display grave changes.

(I) Vital stains invariably enter the cells damaged by alloxan diabetes, though these cells do not accumulate dyes when normally functioning. (II) In most cases the uptake of the vital dye (diffuse staining of the cytoplasm, nuclear staining) took place only after usual methods had already shown cell lesion. In some instances, however, the cell lesion becomes earlier manifest on vital staining. (III) Dyes do not pass into the cells with the same intensity. Niagara sky blue appears in the cells 5 minutes after administration, whilst trypane blue less readily (6 hours) and Evans blue still later. — (IV) The affinity to vital dyes of various regressive changes and destroyed cells is different. — (V) Vital staining is an adequate method to demonstrate the regressing elements of *Langerhans'* islets in alloxan diabetes.

Pathologic Anatomy of Multiple Congenital Arthrogryposis

I. Fleischmann

(2nd Dept. of Pathological Anatomy, Medical University, Budapest)

Multiple arthrogryposis is a congenital developmental anomaly, characterized by limited motility of the joints. The members display characteristic flexion and extension contractures. Some authors attribute a prominent role to the thickening of the articular capsule, others believe the condition to be due to muscle dystrophy or to regressive changes in the central nervous system. As aetiologic factors, inflammation occurring during foetal life, compression of the muscles, and underdevelopment of the foetus should be taken into consideration. 3 cases have been examined post mortem within a year. In one of them spina bifida aperta, in two other cases myocardial fibrosis was present. The role of intrauterine inflammations is emphasized.

Spondylitis due to Fungus Infection

J. Kepes, D. Áfra

(State Scientific Institute of Neurosurgery)

In a 57 years old woman the destruction of the 12th dorsal vertebra occurred according to clinical and X-ray findings, in consequence of a metastatic tumour. The specimen obtained at operation contained a caseous tissue with many giant cells. Mycobacteria could not be detected, but there were in the tissue a great number of structures displaying a double contour. Some of them contained endospores, morphologically corresponding to Coccidioides immitis. This claim, however, could not be proved from the biopsy material by culture. As animal coccidioidomycosis has already occurred in Hungary, it is advisable to produce coccidioidin for diagnostic purposes and proper drugs for therapy.

A Case of Generalized Thrush Septicaemia

Magda Scholz, F. Gerlóczy, K. Schmidt

(2nd Dept. of Pathological Anatomy, 1st Dept. of Paediatrics, Medical University, Budapest)

Conditions under which the apathogenic thrush fungus becomes pathogenic, the processes due to its spread, and the mechanism of its generalization are discussed. Literary data and the authors' own observations suggest that antibiotic treatment is responsible for the increasing incidence of thrush cases. The case reported is the 11th published one of thrush septicaemia in which the kidney was involved, but the first one of isolated thrush of the pyelon. There is undoubtedly some correlation between the growth of thrush and antibiotic therapy. The chief factors, however, are infantile atrophy and exsiccation.

Experimental Interstitial Plasmacellular Pneumonia

L. Brandstein, Anna Csillag

(László Hospital, and State Hygienic Institute, Budapest)

In 5 of 7 cases, a fungus belonging to the order Endomycetales and the genus Saccharomycetaceae was isolated from the lung of infants who died of interstitial plasmacellular pneumonia. By means of the cultures it was possible to produce both *in vivo* and *in vitro*, a structure identical to the one held by *Jirovec* the sporogonium of the protozoon Pneumocystis carinii, generally considered the causative agent of the disease. According to our studies, this form is not a sporogonium, but the ascus of the isolated fungus.

By aspiration of a suspension of the fungus only newborn animals could be infected. Newborn mice developed a clinical pattern resembling the one common in infants. The lungs of

the animals, the majority of which had died spontaneously, exhibited a histological picture very similar to that occurring in infants.

Silver impregnation revealed that the foamy substance filling the alveoli is made up of the vegetative forms, asci and ascospori, of the fungus.

Histological and Clinical Comparative Examination of Rheumatic Activity in Mitral Stenosis

J. László, F. Robicsek, A. Temesváry

1 st Dept. of Pathological Anatomy and Dept. of Postgraduate Surgical Education, Medical University, Budapest)

In 1oo cases of mitral stenosis commissurotomy was carried out. The left auricle was removed and examined histologically. Subendocardially and in the muscle layer there were inflammatory changes in 65 per cent of the cases. Partly round cell foci, partly *Aschoff*'s nodules, the latter associated with alteration of the subendocardial collagen connective tissue, were revealed. A comparison of these findings with the clinical data resulted in the following conclusions.

(i) Where mitral stenosis was attended by clinical symptoms of active rheumatism, rheumatic myocarditis was invariably present. — (ii) In numerous cases there was no symptom of rheumatism, yet the muscle layer of the auricle contained rheumatic nodules. — (iii) In histologically active cases postoperative rheumatic phenomena and complications occurred in a great number. — (iv) The present clinical methods (sedimentation rate, haemoglobin content, leucocyte count, antistreptolysin titer, etc.) are not always suitable for revealing latent active rheumatism. — (v) The results allow conclusions as to the prognosis of heart operations.

New Methods to Produce Experimental Changes in the Aorta

Edit Beregi

(2nd Dept. of Pathologic Anatomy, Medical University, Budapest)

Various methods were employed to produce changes in the aorta of rabbits. *1.*15 animals were given large doses of pilocarpine subcutaneously. The rabbits were killed after 60 to 90 injections. *2.*6 rabbits were sensitized to horse serum, then treated for 70 days with low doses of pilocarpine. *3.*5 rabbits were given gradually increasing doses of physostigmine. 170 injections were administered. *4.* A gauze stripe saturated with terpineol was placed on the frontal cortex of 9 rabbits. They were killed after from 1 to 6 month.

The changes in the aorta were similar in all series : disintegration and destruction of the elastic fibres, oedema, mucoid degeneration, in some cases lipoid and lime deposits, and osteoid formation occurred. In some other cases connective tissue formed in the aortic wall.

Adrenalin-type Arteriosclerosis Induced Experimentally by Coarctation of the Aorta in Rabbits

G. Lusztig, J. Ormos, Á. Botos, B. Korpássy

(Dept. of Pathological Anatomy, Dept. of Experimental Surgery, Medical University, Szeged)

It was observed at the necroscopy of three young patients that coarctation of the aorta is accompanied by severe sclerotic changes in the part above the stenosis. It was therefore tried to bring about arteriosclerosis in rabbits by compressing the abdominal aorta above the coeliac artery by means of a metal clamp. — Coarctation was brought about in 12 rabbits weigh-

ing 2,5 kg on the average. The animals were killed on the 16th to 48th day after operation. In ten of these sclerotic changes of the adrenalin type have developed, i. e. circumscribed dilatations with thinning and hardening of the vessel wall. In all cases but one the changes occurred in the part above the coarctation only ; in one animal sclerosis was found also below the stenosed part. Severe changes were present in 5, mild ones in the other 5 animals. Histologically, there were lime foci in the media. During their life, the animals in which sclerosis was found had displayed a blood pressure elevated by about 30 to 40 mm. Elevated blood pressure did not occur in the rabbits in which no sclerotic change developed. — The mechanism of the changes will be studied in further experiments.

Fibrocystic Disease of the Pancreas

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(1st Dept. of Pathological Anatomy, Medical University, Budapest)

4 cases of fibrocystic disease of the pancreas are reported. The first patient, a newborn infant 5 days of age, died of peritonitis due to perforation following meconium ileus. The second one, a 3 month old infant, died from suppurating bronchopneumonia. A 3 weeks old infant suffered from the same process. The death of a 7½ month old infant was due to asthmatic bronchitis and bronchopneumonia. In one of these cases could only the disease of the pancreas be recognized during life while in the three others diagnosis could not be established before the microscopic examination. In the literature, occasional hereditary factors, fatal infections, deficiency of vitamin A and secretin, alimentary damages, Rh incompatibility and, recently, disorders of the vegetative nervous system, are mentioned as aetiologic agents. The origin of the reported cases could not be traced.

Correlation of Bronchiectasis with Fibrocystic Changes in the Pancreas

K. Farkas

(Uzsoki-street City Hospital, Budapest)

The pancreas was examined in 65 cases of emphysema and bronchiectasis, and in 18 cases of bronchial asthma. In 20 cases the salivary glands have also been examined. Both in the pancreas and in the salivary glands, characteristic but non-specific changes were revealed, such as fibrosis, either diffuse or around the ducts, dilatation of the ducts, desquamation, inspissation of the excreted juice, formation of concrements, cyst formation, and gross or microscopic necroses. In cases of »asthma death« there were in the ducts and in the bronchi structures consisting of mucus and epithelial cells. The same picture was, however, found also in some cases of emphysema and bronchiectasis. As for the morphogenesis, the process resulting in bronchiectasis and in fibrocystic changes in the pancreas results from a disturbance of secretion and the inspissation of the secreted juice. Secretion being dependent on the function of the vegetative nervous system, the ultimate cause of the condition is very likely a vegetative dystonia.

Hyaline Membranes Occurring in Infants' Lungs

Erzsébet Hársfalvy, F. Incze

(2nd Dept. of Pathologic Anatomy, Medical University, Budapest)

According to literary data, the hyaline membrane is not a pathologic entity, is occurring with various diseases and in consequence of various causes. We have found it associated with pneumonia and pulmonary oedema and we believe that it consists of a substance precipitated

from inflammatory exudate or oedema fluid containing protein. The tendency of some exudates to form a membrane may be due to the protein composition of the serum. (In one case the serum globulin level was high). Precipitation might also be induced by some change in the respiration mechanism. Old membranes may be accompanied by homogenization of the alveolar wall.

Expansion Capacity of the Lungs after Death

E. Berki

(Dept. of Pathological Anatomy, Medical University, Pécs)

The capacity to expand on lowering the outer pressure was examined in lungs placed into a closed fluid space allowing to estimate the air content of the lungs or their parts. As a rule, the expansion capacity of the lung was proportional to its air content (spec. gravity). Yet the expansion capacity is lower than that corresponding to the air content in premature infants, interstitial pneumonia, and induration due to statis.

Pathogenesis of Fulminant Hepatitis

I. Sümegi, L. Goreczky, J. Molnár, I. Róth

(State Railway Hospital, Budapest)

Out of 13 patients suffering from hyperacute infectious hepatitis, 4 died between the 2nd and 5th days, and 5 within the first 10 days of the disease. Microscopical examination revealed that in this short time complete destruction of the liver occurred. In the history of 9 patients was previous liver damage mentioned such as syphilis, arsenobenzole, jaundice, eclampsia. The lesion of the nervous system occurring in the course of such diseases may lead to permanent changes which may, if later the organism is afflicted by other and occasionally different injuries, give rise to new severe dystrophic processes. Regarding the correlations between liver and nervous system, processes like the ones mentioned might have played a role in the cases reported. In order to prove this assumption the authors poisoned rabbits with phosphorus, phenylhydrazine, and hepatotoxic serum. The course of the resulting disease was recorded and nephelogrammes were made. After the health of the animals had been restored a second injury was produced by one tenth of the lethal chloroform dose. Control animals had not been exposed to the first injury but were given the same dose of chloroform only. As early as on the 6th day, necrosis extending to about three quarters of the lobule was seen in the pretreated group, whilst in the lobules of the controls only initial signs of central fibrinoid lobular necrosis occurred. In 12 days two thirds of the pretreated animals died. Their liver displayed complete destruction, whereas in the liver of the control rabbits regeneration prevailed. The experiments demonstrate the significance of previous hepatic lesion. The »second blow« gives rise to a process which runs through the pathway prepared by the first disease at a speed resembling that of a conditioned reflex.

Renal Changes Following Denervation

L. Takács-Nagy, P. Endes

(Koltói Anna Hospital, Budapest)

Bilateral sympathectomy and renal biopsy were performed in an interval of about three months. In the biopsy specimens peculiar changes were revealed consisting in irregularly seated small scars, partly atrophic and partly dilated tubuli, and focal calcification of the tubular epithelium. The changes are believed to be neurogenic, due to the disturbance of renal circulation caused by sympathectomy, because they were equally present in the contralateral kidney unaffected by operation.

Cytomegalic Inclusion Body Disease of the Newborn

B. Kőszegi, I. Piukovich

(Dept. of Pathological Anatomy, Medical University, Szeged)

In 49 newborn and older infants died of developmental anomalies or other conditions the parenchymatous and endocrin organs were examined. In one of them the inclusion body disease first reported by *Jesionek* and *Kiolemenoglou* in 1904 was revealed. The essential morphologic features of the disease are cytomegaly, small basophilic inclusions in the cytoplasm and larger acidophilic ones in the nuclei in the parenchymatous organs, especially the kidneys, liver, and lungs. The aetiologic agent is probably one of the human strains of the salivary gland viruses. In the literature one case only was reported in which diagnosis had been set during life. The case observed was that of a 3 month old infant the necropsy of which revealed a complex developmental anomaly of the heart and the large arteries. It is of particular interest that this was the third case published in which inclusion bodies were found in the ganglion cells of the brain.

SECTIONAL MEETING

IV. Oncology

Teratogenous Effect of Janus Green B on Fertile Hen's Eggs

S. Braun

(Péterfy S.-street, City Hospital, Budapest)

The mode of action of the dye was examined in 786 fertile hen's eggs incubated in normal air space. The most effective dose was 100 microg. kg. applied to the serous membrane of the internal lamina. In 24 hours, the dye accumulated on the yolk membrane, at about 6 mm from the germ centre. In living fertile eggs the dye transforms to a leucobasis after 48 hours of incubation. Developmental anomalies occurred in 90 per cent, a normal embryo in 4.6 per cent underdevelopment in 2 per cent and a dead embryo in 3.4 per cent. Among 27 ducks with developmental anomalies observable with the naked eye there were numerous aged and viable ones seen. As a sign of hypoxia, area vasculosa iriformis, and haemopoietic metaplasia occurred. Severe anomalies were seen in the neural membrane of viable embryos. The most grave one was a cardiacus amorphus, an about pinheadsized amorphous structure containing a pulsating sac filled with blood. This anomaly observed in 10 embryos was in 7 cases associated with hydramnion. On microscopic examination, extensive metaplasia was seen in the parenchymatous organs, especially in the liver and kidneys; the mitochondria were increased in number whilst the filamentous forms disappeared. In the brain considerable cytoarchitectonic changes were demonstrated.

The experiments show that the teratogenic effect of Janus Green B is closely related to its transformation to a leucobasis. Hereby tissue hypoxia is produced attaining its highest teratologic efficiency between the 48th to 62nd hours.

Morphologic Changes in the Organs of the Rat after X-ray Irradiation of the Entire Body

B. Kellner, K. Lannert

(State Institute of Oncology, Budapest, and Dept. of Pathological Anatomy, Medical University, Debrecen)

The authors' previous investigations into the effect of factors enhancing tumour growth were extended to X-rays 600 r, corresponding to about 50 LD, were administered. Generally, the changes were similar to those produced by colchicine, podophyllin, nitrogen mustard and urethane, especially in that they develop in a short time. They are marked after 1 hour, reach their peak after 12 hours and regress after about 3 days. Much resemblance has been found as regards localization: the changes were most marked in the duodenum, the small intestine, the haemopoietic organs, and the testicles. Atypical mitoses were present in great numbers.

In spite of the similarities the action of X-rays differs from that of other factors. First, no complete regression occurs. Connective tissue proliferation begins, especially in the spleen and the lymph nodes, as early as after the first dose. Vascular changes persist as a sign of profound mesenchymal lesion. No apparent increase in the number of mitoses can be demonstrated, pointing to a lack of karyoclastic effect. The chromatin fragments and globules, i. e. the spheroid structures occurring in enormous numbers at times, especially in the duodenum, are not always

seated near fragmented nuclei. In places they lie next to apparently intact nuclei some of which stain less than others. The phase of restitution is characterized by numerous mitoses. It could not be established with certainty in which phase of mitosis the nucleus breaks up. Nuclei are probably equally radiosensitive in all phases of mitosis.

Effect of Acute and Chronic Administration of Urethane on the Organs of the Rats

A. Haraszti, B. Kellner

(Dept. of Pathological Anatomy, Medical University, Debrecen)

105 rats were intraperitoneally treated with a 10 per cent solution of urethane. In order to study the acute effect, a single dose of 0.1 g/100 g body weight was injected. Chronic treatment was carried out twice a week with 0.07/100 g. The most marked damage was observed in the lymphoid organs, duodenum, and testicles. In the lymphoid organs and duodenum the maximum effect lasted for from 6 to 24 hours. In the kidneys and the liver the action was protracted. Changes due to chronic treatment essentially corresponded to the acute lesions, and were considerably milder than those produced by podophyllin, colchicine, or nitrogen mustard. The leucocyte count decreased for 48 hours but by the end of the 3rd day it was normal again. In the differential counts absolute lymphopenia and relative leucocytosis were found. Unlike colchicine, urethane did not bring about destruction of the bone marrow. It has been found that urethane acts not only on dividing but also on resting cells.

Fluorescence Microscopic Examination of Mice Suffering from Spontaneous Tumours and Treated with Cancerogenous Substances

Margit Németh, Gy. Gorácz

(2nd Dept. of Pathological Anatomy, Medical University, Budapest)

In order to study the absorption and distribution of benzpyren in mice with a spontaneous tumour, 20 animals were administered intramuscularly a single dose of 0.2 mg. The animal were divided in 4 groups, each consisting of 5 mice. They were killed on the 2nd, 4th, 6th, and 8th day, respectively. In accordance with the data of literature, the areas showing the most vigorous fluorescence proved sudanophilic. The strongest fluorescence was at the site of the injection ; it was less vivid in the liver and in the tumour. The fluorescence decreased with time. The violet fluorescence given by benzpyren with unchanged molecular structure was observed at the site of the injection only in the 2 and 4 days old cases, whilst at the other places the fluorescence was greenish yellow. The examinations could not settle whether the latter phenomenon was due to decomposition products of benzpyren or to complex compounds formed from benzpyren and some constituents of the organism, both processes being attended by a change in colour and unchanged cancerogenous effect.

Chronic Local Irritation and Chemical Cancerogenesis

Márta Mosonyi, Anna Sztanojevits, A. Traub, B. Korpássy

(Dept. of Pathological Anatomy, Medical University, Szeged)

The much disputed problem of the correlation of local irritation and chemical carcinogenesis can best be studied by applying cancerogenic compounds with a marked remote effect showing itself by the production of tumours in different organs. 2-acetylaminofluorene is a compound corresponding to this demand. Local irritation was produced (i) with tannic acid injected subcutaneously. (In previous experiments repeated treatment with tannic acid resulted in local ulcers, gastric erosions and ulcers, acinocentral necroses in the liver, and cirrhosis).

(ii) Laparotomy was performed and a gastric ulcer was produced with thermocauterization of the stomach mucosa. (iii) The intestinal mucosa was exposed to protracted irritation by mixing to the food baryum sulfate, talc, powdered glass. The half of each group received 2-acetylaminofluorene in the food, the rest served as control. No tumour arose from the irritated skin or mucosa. On the 180th day of the treatment 92 per cent of the animals treated with both the compound and tannic acid developed liver tumours, in some cases a malignant (metastasizing) one. In the group treated with 2-acetylaminofluorene alone a considerably lower percentage, 28 per cent displayed tumours in the liver.

Effect of Tumours on the Phagocytic Activity of Leucocytes

G. Vajda, L. Goreczky, I. Róth, I. Sümegi

(State Railways Hospital, Budapest)

In the course of investigations into tumour immunity it had been found that no intense phagocytosis of tumour cells can be elicited by immune sera. The tumour cell proved toxic to mice. In the present experiments the effect of tumours on the cellular system was examined in *vivo* and in *vitro*. Extracts of *Brown—Pearce*, *Guérin* and human tumours were mixed to rat, rabbit, and human leucocytes and their phagocytic activity was estimated by Wright's and Platonov's modified methods. The results have uniformly shown that tumour extracts decrease the phagocytic activity of leucocytes. The mean degree of inhibition is 29 per cent with Brown Pearce tumours, 33 per cent with Guérin's cancer, and 39 per cent with human tumours. Owing to this effect, the cellular defensive mechanism of the organism against tumours may also be inhibited.

Further Contributions to the Effect of Isonicotinic Hydrazide Exerted on the Organism and Tumour Growth in Experimental Animals

T. Tiboldi, P. Molnár, Margit Dávid, K. Kovács

(Dept. of Pathological Anatomy, Medical University and City Hospital, Szeged)

In earlier experiments the administration of INH to rabbits suffering from a Brown—Pearce tumour resulted in increased malignancy. Next the parenchymatous and endocrin organs of the animals were examined for micrometastases. The data obtained corroborated the above observation. Subsequently, the histophysiology of endocrine glands, and the number of circulating eosinophils were studied in rats treated with INH. Under the experimental conditions no hyperactivity of the hypophyseo-adrenocortical system occurred. The parenchymatous organs exhibited no toxic changes.

Does Isonicotinic Acid Hydrazide Increase Tumour Malignancy?

Gy. Berencsi, A. Entz, Á. Vajkóczy

(State Tuberculosis Sanitarium, Debrecen)

The problem, that INH may occasionally increase the malignancy of tumours has been repeatedly mentioned. First the question was examined whether or not INH promotes the development of coal tar cancer. In male rabbits treated simultaneously with coal tar and INH no such effect was observed. Next it was tried to influence the metastasis formation of coal tar cancer. The experiments have not yet been concluded. It seems, however, that INH exerts no unfavourable action in this respect either.

Simultaneous Occurrence of Tuberculosis and Cancer in the Stomach

Éva Gáthy

(State Institute of Oncology, Budapest)

In the stomach of a 62 years old woman removed for tumour, there was a prepyloric ulcer with elevated margins. On the serosa surface an almond-sized and several smaller lymph nodes were seated. Histology revealed typical adenocarcinoma and typical tubercles in the muscle layer. In the lymph nodes no cancer metastasis, but typical tubercles were found.

Changes in the Lymph Nodes during Carcinogenesis due to Butter Yellow

K. Lapis

(State Institute of Oncology, Budapest)

The following changes have been observed in the course of butter yellow treatment. (i) Progressive decrease in amount of the pulpa, especially of the lymphoid tissue. (ii) Broadening of the sinus system. (iii) Proliferation, then desquamation of the sinus endothelium and reticulum. (iv) Plasmacellular transformation of the pulpa. (v) Erythrocyte phagocytosis and accumulation of iron pigment in the histiocytoid elements of the sinuses and the pulpa.

These observations are in agreement with those of Parsons et al., made after transplantation of tumours into mice or during the carcinogenetic action of various hydrocarbons. The changes observed are in many respects similar to those found by *Korpássy* in the lymph nodes of rats treated with tannic acid.

Since all lymph nodes are involved, the effect is considered a systemic one.

The effect of hydrocarbons obeserved by Parsons is twofold, (i) inhibition of lymphocyte production, (ii) promotion of myeloid proliferation. The same twofold effect seems to be exerted by aminobenzene derivatives.

The changes described developed in both groups of animals, both in which a cancer has developed and in which there was no tumour. The changes are therefore probably due to the effect of the cancerogenic agent rather than to the tumour and they seem to have no significant role in the susceptibility to tumours.

Malignant Breast Tumours in Males

Gy. Gonda

(László Hospital, Budapest)

In the biopsy and necropsy material of three large hospitals the participation of male patients in breast cancer was 1 in 100. In 7 own cases the cancer was mostly of the medullary type, in contrast with the data of literature. A rare case of *Paget's* carcinoma was also observed. Regarding the pathogenesis of the male breast cancer, histologic examination is imperative in all suspicious cases of posttraumatic condition or apparent eczema. Malignant cases should be early and radically operated on.

Correlation of Topography and Structure of Basal Cell Cancers

I. Fodor, I. Betléri

(Uzsoki-street, City Hospital, Budapest)

Examination of 787 specimens of basal cell skin cancer revealed no correlation between the structure of the tumour and the region of occurrence. Similarly, no correlation was found between structure and malignancy ; malignant basal cell cancers may be developed from any type. As to the onset *Krompecher's* original conception is thought to be correct.

Relationship of Gall Stones and Gall Bladder Cancer

L. Podhragyay

(Uzsoki-street, City Hospital, Budapest)

Gall stones occurred in 238 (9 per cent) of 2771 necropsies. In 25 (10 per cent) of the stone cases a cancer was also present. Examined were further 346 gall bladders removed by operation. In this group, 34 calculous gall bladders (10 per cent) and among them 2 cancerous ones were observed. Among the cases of cancer, the proportion of those with a gall stone and those without one was 27 to 13. As to sex, 57 per cent of the patients were females, 43 per cent males. The averege age was for stone and cancer 64 years, for operated cholelithiasis 49 years. In the necropsy material the incidence of cancer of the gall bladder and bile ducts was 1.2 per cent.

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